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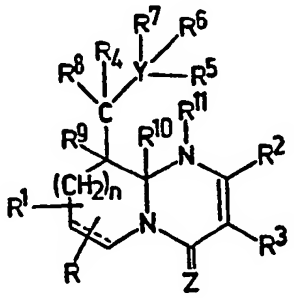
(54) 4-oxo-nitrogen bridgehead compounds

(57) Nitrogen bridgehead compounds of the general formula (I)



(I)

[wherein
R is H, alkyl or alkoxycarbonyl
R^1 is H or alkyl; or
R and R^1 together form
$—(CH=CH)_2—$
R^2 is H, halogen, alkyl, phenyl or a 5- or 6-membered heterocyclic saturated ring,
R^3 is H, optionally substituted phenyl, acyl, carboxy, alkoxycarbonyl —CN, carbamoyl, alkylcarbamoyl, alkyl, alkanoylcarbamoyl, acid-hydrazido, or
—CO—NH—N=C (R^{12} R^{13}) (wherein R^{12} and R^{13}) are alkyl, carboxyalkyl, alkoxycarbonyl-alkyl or phenyl) or
R^2 and R^3 form $—(CH_2)_t$ (t is 3 or 4)
Z is oxygen and
n is 0, 1 or 2 and
a) if R^{11} is H and R^9—R^{10} and R^7—R^8 form chemical bonds then
R^4 is H or phenyl,
YR^5R^6 represents oxygen or
Y represents nitrogen and
R^5 is alkyl optionally substituted by hydroxy, carboxy or alkoxycarbonyl or phenyl optionally substituted by nitro, alkyl, alkoxycarbonyl and/or halogen; mono- or bi-cyclic nitrogen-containing heteroaryl, hydroxy aminothiocarbonyl, aminothiocarbonylamino or phenylamino,
R^6 represents an unshared electron-pair, or H or alkyl, and in these two cases a salt is formed or
R^5 and R^6 form $—(CH_2)_p—$ (p is 4 or 5) and a salt is formed with N+ or
b) if R^9 is H and R^{10}—R^{11} and R^8—R^7 form chemical bonds, then R^4, R^5, R^6 and Y are as given under item (a); or
c) if R^8—R^9 and R^{10}—R^{11} form chemical bonds, then
R^4 is H or phenyl,
$YR^5R^6R^7$ represents halogen, or YR^6R^7 represents oxygen
and R^5 is H or alkyl; or
YR^6R^7 represents sulfur
and R^5 is cyano; or
Y represents nitrogen
and R^5 is alkyl optionally substituted by hydroxy, carboxy, or alkoxycarbonyl; phenyl optionally substituted by nitro, C_{1-4} alkyl, alkoxycarbonyl and/or halogen; or mono- or bicyclic nitrogen containing heteroaryl,
R^6 is H or alkyl, or
R^4 and R^6 form $—(CH_2)_m—$ (m is 3 or 4) or
R^5 and R^6 form $—(CH_2)_p—$(p is 4 or 5) and
R^7 represents an unshared pair of electrons] and the tautomers and salts thereof.

The novel compounds possess physiological activity.

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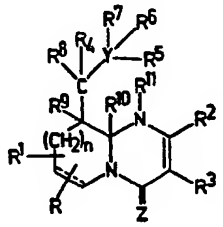
SPECIFICATION

Nitrogen bridgehead compounds, the salts thereof, processes for their preparation and pharmaceutical compositions containing them

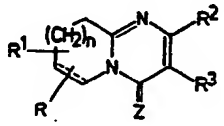
The present invention relates to nitrogen bridgehead compounds, the salts thereof, processes for their preparation and pharmaceutical compositions containing them.

The new nitrogen bridgehead compounds have the general formula:



(I)

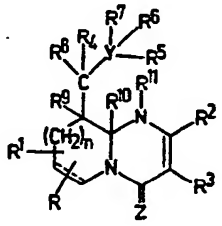
We have unexpectedly found that compounds of the general formula



(II)

contain active hydrogens in the methylene group beta to the nitrogens and these active hydrogens are suitable for electrophilic substitution reactions.

According to one feature of the present invention there are provided compounds of the general formula (I)



(I)

[wherein

R represents hydrogen, C_{1-4} alkyl or alkoxycarbonyl containing 1—4 carbon atoms in the alkoxy moiety;

R^1 represents hydrogen or C_{1-4} alkyl; or

R and R^1 together form $—(CH=CH)_2—$ being attached to the two adjacent ring-carbon atoms in which case the dotted line represents a carbon-carbon bond,

R^2 represents hydrogen, halogen, C_{1-4} alkyl, phenyl or a 5- or 6-membered monocyclic heterocyclic saturated ring;

R^3 represents hydrogen, optionally substituted phenyl, C_{1-4} acyl e.g. alkanoyl, carboxy, alkoxycarbonyl containing C_{1-6} alkoxy, nitrile, carbamoyl, alkylcarbamoyl, alkyl; C_{1-4} alkanoyl substituted carbamoyl, acid-hydrazido, (—$CONHNH_2$) or —CO—NH—N=$C(R^{12}R^{13})$ (wherein R^{12} and R^{13} which may be the same or different, each represents C_{1-4} alkyl or carboxyalkyl or alkoxycarbonyl-alkyl or phenyl),

or

R^2 and R^3 form together $—(CH_2)_t$ (wherein t is 3 or 4),

Z represents oxygen and

n is 0, 1 or 2 and

a) if R^{11} is hydrogen and R^9 and R^{10} together and R^7 and R^8 together each form a chemical bond then R^4 stands for hydrogen or phenyl,

Y represents an oxygen atom without its lone pairs of electrons, in which case R^5 and R^6 each represents a lone pair of electrons; or

Y represents a nitrogen atom without its lone pair of electrons and

R^5 represents C_{1-4} alkyl optionally substituted by hydroxy, carboxy or alkoxycarbonyl containing C_{1-6} alkoxy or phenyl optionally substituted by one or several nitro, C_{1-4} alkyl, or alkoxycarbonyl containing C_{1-6} alkoxy, and/or halogen; mono- or bicyclic nitrogen-containing heteroaryl, hydroxy, aminothiocarbonyl, aminothiocarbonylamino or phenylamino,

R^6 represents an unshared electron-pair, hydrogen or C_{1-4} alkyl, and in these two cases a salt is formed between the positive nitrogen and an anion, or
R^5 and r^6 together form —$(CH_2)_p$ (wherein p is 4 or 5) and a salt is formed with the positive nitrogen; or
b) if R^{10} and R^{11} together form a chemical bond and R^9 stands for hydrogen, R^8 and R^7 together form a chemical bond, then R^4, R^5, R^6 and Y are as given under item (a); or
c) if R^8 and R^9 together, and R^{10} and R^{11} together each form a chemical bond, then R^4 represents hydrogen or phenyl, and
Y, R^5, R^6, R^7 together form a halogen atom; or
Y represents an oxygen atom without its lone pairs of electrons,
R^6 and R^7 each represents an unshared electron-pair, and
R^5 represents hydrogen or C_{1-4} alkyl; or
Y represents a sulfur atom without its lone pairs of electrons,
R^6 and R^7 each represents a lone pair of electrons, and
R^5 is cyano; or
Y represents a nitrogen atom without its lone pair of electrons,
R^5 represents C_{1-4} alkyl optionally substituted by hydroxy, carboxy, or alkoxycarbonyl or phenyl optionally substituted by nitro, C_{1-4} alkyl, or alkoxycarbonyl containing C_{1-6} alkoxy, and/or halogen mono- or bicyclic nitrogen containing heteroaryl,
R^6 represents hydrogen or C_{1-4} alkyl, or
R^4 and R^6 together form —(CH_2)m— wherein m is 3 or 4, or
R^5 and R^6 together form —$(CH_2)_p$— wherein p is 4 or 5, and
R^7 represents an unshared pair of electrons] and the tautomers and salts thereof.

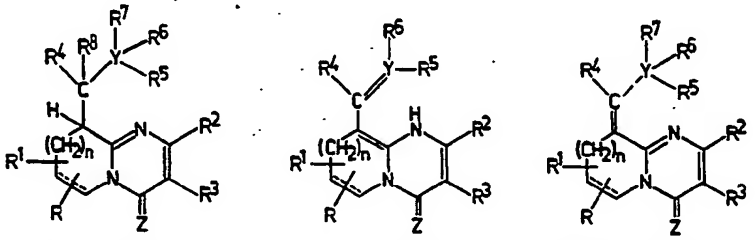
Where a salt is formed with a positive nitrogen the anion is preferably a halide ion.

The compounds of the present invention serve as starting materials for the preparation of interesting physiologically active compounds, and moreover, in general, possess interesting physiological activity *per se*.

Thus the bridgehead compounds of the general formula I and certain compounds prepared therefrom may be of interest in therapy.

The prepared compounds of the general formula I may exist in three tautomeric forms:

Fig. 1



All such forms of the compounds of formula I and salts thereof are within the scope of the present invention.

Depending upon the nature of the substituents one or another tautomeric form amy predominate, or two tautomeric forms under given circumstances may form an equilibrium mixture which may be shown by spectroscopic methods. Each tautomeric form may also exist in the form of Z—E geometric isomers. In the Examples the prepared products are named according to the prevailing tautomeric form.

The present invention includes all the possible geometric isomers and racemic and optically active forms of the nitrogen bridgehead compounds of the general formula I.

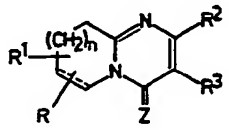
It will be appreciated that the dotted line present in the 6,7-position may, if, desired, represent a carbon-carbon bond so that either a single carbon-carbon bond or a double carbon-carbon bond may be present in a 6—7 position.

In general a single carbon-carbon bond is present in the 6,7-position except where R and R^1 together form the group —$(CH{=}CH)_2$ in which case a double carbon-carbon bond is present e.g. for aromaticity.

Preferred compounds of the present invention include compounds of general formula I wherein n is 0. Compounds of general formula I wherein n is 1 are also preferred. Also preferred are those compounds of the formula I wherein R and R^1 stand for hydrogen or R represents C_{1-4} alkyl, particularly methyl e.g. in the 6-position and R^1 is hydrogen or C_{1-4} alkyl, preferably methyl.

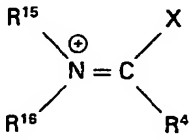
In the compounds of formula I R^2 preferably represents hydrogen, halogen, phenyl or a 5- or 6-membered saturated monocyclic heterocyclic ring. Where R^5 is present this group is preferably pyridyl, hydroxy, aminothiocarbonyl, aminothiocarbonylamino or phenylamino.

According to the invention compounds of general formula I (as hereinbefore defined) and the tautomers and salts thereof may be prepared by reacting a nitrogen bridgehead compound of the general formula



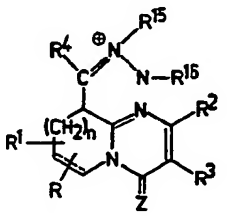
(II)

wherein R, R^1, R^2, R^3, Z, n and the dotted line are as given above
a_1 with an imminium salt of the general formula



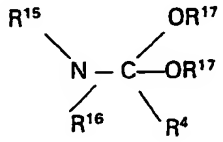
(III)

wherein R^4 stands for hydrogen or phenyl,
R^{15} stands for alkyl optionally substituted by hydroxy, carboxy, or alkoxycarbonyl containing C_{1-6} alkoxy, phenyl or optionally substituted by one or several nitro, C_{1-4} alkyl, or alkoxycarbonyl containing C_1 alkoxy, and/or halogen or mono- or bicyclic nitrogen containing heteroaryl, preferably pyridyl,
R^{16} stands for hydrogen or C_{1-4} alkyl or
R^4 and R^{16} together form $-(CH_2)_m-$ wherein m is as given above or
R^{15} and R^{16} together form $-(CH_2)_p-$ wherein p is as given above,
X represents halogen or C_{1-4} alkoxy,
A is an anion
and thus nitrogen bridgehead compounds of the general formula



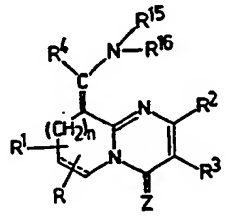
(Ia)

are obtained — wherein R, R^1, R^2, R^3, R^4, R^{15}, R^{16}, A, Z, n and the dotted line are as defined above, or a_2 with a diacetal of the general formula



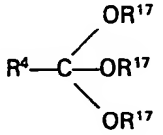
(IV)

wherein R^4, R^{15}, R^{16} are as given above and R^{17} is C_{1-4} alkyl and thus nitrogen bridgehead compounds of the general formula



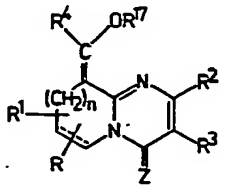
(Ib)

are obtained, wherein R, R^1, R^2, R^3, R^4, R^{15}, R^{16}, Z, n and the dotted line are as defined above, or a_3 with a trialkyl ester of orthocarboxylic acid of the general formula



(V)

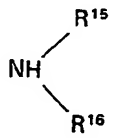
wherein R^4 and R^{17} are as defined above, and thus nitrogen bridgehead compounds of the general formula



(Ic)

are obtained, wherein R, R^1, R^2, R^3, R^4, R^{17}, Z, n and the dotted line are as given above, or

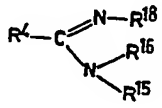
a_4) with an amine of the general formula



(VI)

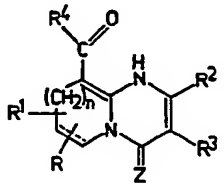
wherein R^{15} and R^{16} are as defined above and with the trialkyl ester of the orthocarboxylic acid of the general formula V — wherein R^4 and R^{17} are as defined above and thus nitrogen bridgehead compounds of the general formula Ib are obtained — wherein the substituents are as defined above, or

a_5) with an amidine of the general formula



(VII)

wherein R^4, R^{15} and R^{16} are as defined above and R^{18} is phenyl and thus compounds of the general formula Ib are obtained — wherein the substituents are as given above — and by converting, if desired, a compound of the general formula Ia, Ib, Ic or Id



(Id)

obtained by any of the above methods into another compound of the formula Ia, Ib, Ic, Id or I and, if desired, converting R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, or Y in the obtained compound of the general formula I into another R^2, R^3, R^4, R^5, R^6, R^7, R^8, R^9, R^{10}, R^{11}, or Y in optional order and/or resolving an obtained racemate and/or converting it to a pharmaceutically suitable salt or setting it free from its salt.

The term "C_{1-4} alkyl" used hereinafter stands for a straight or branched alkyl such as methyl, ethyl, n-propyl, isopropyl, etc. The "optionally substituted phenyl" term may stand for a phenyl substituted by one or several, same or different substituents, such as C_{1-4} alkyl, C_{1-4} alkoxy, amino, hydroxy, carboxylic acid, carboxylic acid derivative, nitro, or halogen. The term "C_{1-4} alkoxy" inlcudes straight or branched alkyl containing alkoxy. The term "carboxylic acid derivative" may stand for alkoxycarbonyl containing C_{1-4} alkoxy, nitrile, aminocarbonyl optionally substituted by C_{1-4} alkyl, C_{1-4} alkanoyl, (C_{1-4} alkyl containing dialkylamino-methylene)-amino substituted on the amino group or carbohydrazido. The "optionally substituted heteroaryl group" may include monocyclic or bicyclic compounds containing one or several, same or different heteroatoms, optionally substituted by alkyl, nitro, alkoxy, amino group or groups and halogen(s) (such as pyridyl).

The heterocyclic compounds of the general formula II used as starting materials may be prepared by the methods disclosed in Hungarian patent specifications Nos. 156,119, 158,085, 162,384, 162,373 and 166,577 and Dutch patent specification No. 7,212,286 and compounds of the formulae III—VII used as reactants or compounds used for the preparation thereof are products commercially available.

Imminium salts of the general formula III used in method a_4) may preferably be prepared in situ from the corresponding acid amide derivative by using acid halide or ester used for quaternation.

As an acid halide phosphoroxychloride, phosgene, thionyl chloride, phosphorus pentachloride, aluminium trichloride, organic acid chlorides, sulfonic acid chlorides, phosphoroxybromide and other acid halides may be used.

As ester derivatives dialkyl sulfates, alkyl halides, alkyl sulfonates (such as alkylbenzenesulfonate, alkyl-p-toluene-sulfonate, etc.) trialkylphosphate, trialkyl oxoniumfluoroborates may be employed.

As acid amide, derivatives N,N-dimethylacetamide, N,N-dimethylformamide, N-methyl-N-phenylformamide, N,N-diethylbenzamide, N-formyl-poperidine, benzanilide, formanilide, 1-methyl-2-pyrrolidinone and other acid amide derivatives are preferred.

The reaction may be carried out in an excess of the used acid amide or in the presence of an inert solvent. As inert solvents hydrocarbons, preferably benzene, toluene, halogenated hydrocarbons, preferably chloroform, dichloromethane, dichloroethylene, o-dichlorobenzene, chlorobenzene, ethers, preferably dioxan, tetrahydrofuran may be employed. The reaction is carried out at —10—200°C, preferably at 0—100°C.

The reaction may be performed by adding dropwise a solution of the compound of the general formula II dissolved optionally in an acid amide or inert solvent to the mixture of acid amide-acid halide or alkylating agent diluted, if desired, with a suitable inert solvent, preferably at a temperature of 0—50°C. In order to complete the reaction the mixture is stirred at 50—200°C, preferably at 50—120°C. The reactants may preferably be added in a different order, too. The reaction mixture may be further worked up by evaporating the reaction mixture at reduced pressure, by treating the residue by a suitable solvent and by removing the obtained crystalline nitrogen bridgehead compound of the general formula Ia by filtration.

One may also proceed by converting the formed nitrogen bridgehead compound of the general formula Ia to a different compound of the general formula I without isolation. The reaction mixture is poured to icy water or to a cooled alcohol solution followed by pouring the alcohol solution to icy water. The pH of the aqueous solution is adjusted to neutral and when using an inert solvent the organic and aqueous layers are separated or the aqueous part is shaken out with a water-immiscible solvent. The organic solvent is dried and evaporated at reduced pressure. The obtained crude nitrogen bridgehead compound of the general formula I is crystallized from a suitable solvent.

If as a solvent an excess amide is used the compound of the general formula I may precipitate after pouring on water in the form of crystals and may be removed by filtration.

According to the embodiment of the process variant a_2/ a nitrogen bridgehead compound of the general formula II may be reacted with the diacetal of the general formula IV without any solvent or in the presence of an inert solvent at 20—200°C, preferably at 60—160°C under heating.

As inert solvents hydrocarbons (preferably benzene, toluene, xylene) or chlorinate hydrocarbons (pref. chloroform, chlorobenzene, dichloromethane etc.), nitriles (acetonitrile etc.) may be used.

The reaction may preferably last for 1.0—20 hours.

The crude nitrogen bridgehead compound of the general formula Ib obtained after evaporation, preferably at reduced pressure, is recrystallized from a suitable solvent and the compound of the general formula Ib may be transformed, if desired, to different compounds of the general formula I by methods known per se.

When carrying out process variant a_3/ the nitrogen bridgehead compound of the general formula II is reacted with orthocarboxylic acid trialkyl ester of the general formula V preferably in the presence of an acid anhydride, optionally of a Lewis acid.

As acid anhydrides preferably acetic acid anhydride or propionic acid anhydride may be used, but other acid anhydrides may also be employed. As Lewis acid the conventional agents may be employed, such as aluminium chloride, zinc chloride, aluminium bromide, borotrifluoride, irontribromide and other Lewis acids.

The reaction may be carried out at 50—200°C. Related to 1 mole of nitrogen bridgehead compound of the general formula II 0.9—10.0 mole of orthocarboxylic acid triethylester and 5—100 moles of acid anhydride may be used.

The reaction time depends on the reactants and on the reaction temperature. It may vary between 5 hours to 30 hours. The reaction mixture is evaporated at reduced pressure. The residue is crystallized from a suitable solvent.

The nitrogen bridgehead compound of the general formula II is reacted according to method a_4/ with an amine of the general formula VI and with orthocarboxylic acid trialkyl ester of the general formula V optionally in the presence of a Lewis acid. As Lewis acid the same reactants may be used as given above. The reaction may be carried out at 30 to 200°C. Related to 1 mole of nitrogen bridgehead compound of the general formula II preferably 0.9—10 moles of an amine of the general formula VI, 1.0—10 moles of orthocarboxylic acid trialkylester of the general formula V and 0.1—10 g. of Lewis acid may be employed. The obtained reaction mixture is crystallized from a suitable solvent.

When carrying out process variant a_5/ a compound of the general formula II is reacted with an amidine of the general formula VII, optionally in the presence of a solvent at 80—300°C under heating. The same solvents may be used as in method a_2/.

According to a preferable embodiment of the process 1 mole of the compound of the general formula II is reacted with 0.9—3 moles of an amidine of the form VII. If a solvent is used, the solvent is distilled off after the reaction is completed and the residue is recrystallized from a suitable solvent. If the reaction is carried out without any solvent, the reaction mixture is crystallized from a suitable solvent, when the reaction is completed.

In an obtained compound of the general formula I the following substituents may be converted as follows:

A compound of the general formula I — wherein R^8 and R^9, and R^{10} and R^{11} form a chemical bond, R^4 stands for hydrogen, or phenyl, Y stands for a stripped nitrogen atom, R^7 is an unshared pair of electrons, R^6 stands for C_{1-4} alkyl, R^5 is C_{1-4} alkyl or optionally substituted phenyl — may be
a/ hydrolysed in aqueous medium, and thus compounds of the general formula I are obtained — wherein R^{11} is hydrogen, R^7 and R^8 and R^9 and R^{10} form a chemical bond, R^4 represents hydrogen or phenyl, $Y(R^6,R^5)$ stands for oxygen. The hydrolysis is preferably carried out at a pH different from 7.,
b/ treated with an alcohol-hydrochloride mixture and thus compounds of the general formula I are obtained — wherein R^8 and R^9 and R^{10} and R^{11} form a chemical bond, R^4 is as defined above, Y is a stripped oxygen atom, R^7 and R^6 represent a lone electron-pair and R^5 stands for C_{1-4} alkyl,
c/ the hydrochloride salt of the compound of the general formula I mentioned above may be reacted with an amino compound containing secondary or primary amino group and thus compounds of the general formula I are obtained wherein R^8 and R^9 and R^{10} and R^{11} form a chemical bond, R^4 represents hydrogen or phenyl, Y stands for a stripped nitrogen atom, R^7 is a lone electron-pair and R^5 and R^6 are as defined above under item c/.

As an amine compound ammonia, hydrazine, phenylhydrazine, optionally substituted aromatic amine, aliphatic amine, piperidine, pyrrolidine, amino-pyridines, hydroxylamine, thiosemicarbazide, semicarbazide, guanidine, etc. may be used. The reaction may preferably be carried out in the presence of an alkane carboxylic acid, such as acetic acid or propionic acid, etc.

The latter compound of the general formula I may also be prepared from such compounds of the general formula I — wherein R^{11} stands for hydrogen, R^7 and R^8 and R^9 and R^{10} form a chemical bond, R^4 stands for hydrogen or phenyl, $Y(R^5,R^6)$ stands for oxygen. The same amines may be used as mentioned above.

By treating a compound of the general formula I — wherein R^{11} represents hydrogen, R^7, R^8 and R^9 and R^{10} form a chemical bond, R^4 is hydrogen or phenyl, $Y(R^5,R^6)$ stands for oxygen — with a halogenating agent such compounds of the general formula I are obtained — wherein R^8 and R^9, R^{10} and R^{11} form a chemical bond, R^4 is hydrogen, C_{1-4} alkyl, C_{6-10} aryl, $Y(R^5,R^6,R^7)$ stands for halogen.

As halogenating agents preferably phosphorus trichloride oxide, thionyl chloride, phosphorus tribromide oxide, phosphorus pentachloride, phosphorus tribromide, aliphatic acid halide and optionally suitable mixtures thereof may be used. The reaction may be carried out in an excess of the halogenating agent or in the presence of an inert solvent.

As inert solvents aromatic hydrocarbons, such as benzene, chlorinated hydrocarbons, such as chloroform, dichloromethane, chlorobenzene etc. may be employed.

A compound of the general formula I — wherein R^8 and R^9 and R^{10} and R^{11} form a chemical bond, R^4 stands for hydrogen or phenyl, $Y(R^7,R^6)$ represent oxygen, R^5 stands for C_{1-4} alkyl — is
a/ hydrolysed in aqueous medium giving thus a compound of the general formula I — wherein R^7 and R^8 and R^9 and R^{10} form a chemical bond and R^{11} stands for hydrogen, R^4 stands for hydrogen or phenyl, and $Y(R^6,R^5)$ represents oxygen. Hydrolysis is preferably carried out at a pH different from 7.,
b/ reacted with a secondary or primary amine giving thus a compound of the general formula I — wherein R^8 and R^9 and R^{10} and R^{11} form a chemical bond, R^4 stands for hydrogen or phenyl, Y represents a lone pair of electrons or a stripped nitrogen atom, R^7 stands for an unshared pair of electrons, R^5 stands for C_{1-4} alkyl, optionally substituted phenyl, optionally substituted heteroaryl, hydroxy, aminothiocarbonyl, amino-thiocarbonyl-amino, amino substituted by phenyl, R^6 stands for hydrogen, C_{1-4} alkyl or R^5 and R^6 together form $—(CH_2)_p—$ wherein p is 4, 5.

The new compounds of the general formula I are first of all used as intermediate products of pharmaceutical products. These compounds are reacted with aryldiazonium salts and are converted thus to pyrido(1,2-a)pyrimidines substituted with hydrazono in the 9-position, the latter compounds being end products displaying several useful pharmaceutical activities, such as antiallergic activity. Several representatives of the compounds of the general formula I show themselves PG-antagonistic, analgetic, antiarteriosclerotic, tranquillant or other activities and may be formulated to pharmaceutical compositions.

If the nitrogen bridgehead compounds of the general formula I are used as pharmaceutical compositions then an effective amount of the drug is supplied at a daily dosage level from 1 to 1500 mg. depending on the application field, administered in a single or divided dose.

The compounds of the general formula I may be formulated into forms, such as dragées, tablets, suppositories, injections, capsules, powders or other forms and the conventional additives, disintegrating agents and carriers may be added.

The further details of the invention are illustrated by the following Examples which serve for illustration and not for limitation.

EXAMPLE 1

5.6 g. of phosgene are dissolved in 50 ml. of dichloromethane and to the solution 3.7 g. of dimethylformamide are dropped at 5 to 10°C. To the obtained suspension a solution of 11.8 g. 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido(1,2-a)pyrimidine in 20 ml. of dichloromethane is added dropwise at 30—35°C and after stirring for 2 hours the solvent is distilled

off. The residual solid is suspended with ether, the undissolved crystals are filtered and dried. 15.2 g. (93%) of 3-ethoxycarbonyl-6-methyl-9-[/dimethyl-imino/-methyl]-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine chloride are obtained, melting point: 211°C (decomposition).

Analysis for the formula $C_{15}H_{22}N_3O_3Cl$

calculated: C 54.96%; H 6.77%; N 12.82%; Cl 10.82%;
found: C 55.08%; H 6.81%; N 12.78%; Cl 10.90%;

EXAMPLE 2

15.2 g. of 3-ethoxycarbonyl-6-methyl-9-[/dimethylimino/-methyl]-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine chloride are suspended in 40 ml. of 20% by W/V aqueous solution of sodium carbonate. The precipitated crystals are filtered and dried. 11.5 g. (85%) of 3-ethoxycarbonyl-6-methyl-9-/dimethylamino-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are obtained, after recrystallization from ethanol the product melts at 135—137°C.

Analysis for the formula $C_{15}H_{21}N_3O_3$

calculated: C 61.84%; H 7.27%; N 14.42%;
found: C 61.52%; H 7.33%; N 14.29%;

EXAMPLES 3 TO 10

10.0 mmoles of a starting material as given in Table 1 are dissolved in 7.3 g. of dimethylformamide and 3.1 g. of phosphorus trichloride oxide are added to the reaction mixture at 15—20°C. The reaction mixture is stirred for 2 hours at room temperature and poured to 30 g. of ice. The pH of the obtained solution is adjusted to 6—6.5 by the addition of a 20% by W/V aqueous solution of sodium carbonate. The precipitated solutions are filtered, washed with water, dried and crystallized. The obtained substances and characteristic data thereof are shown in Table 1.

TABLE 1

No. of Example	Starting material	Obtained product	Yield	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found C%	H%	N%
3.	3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido-[1,2-a]pyrimidine	9-/dimethylamino-methylene/-3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-pyrido/1,2-a/-pyrimidine	76	136–137	ethanol	$C_{15}H_{21}N_3O_3$	no melting point depression when admixed with the product of Example		
4.	3-carboxy-6-methyl-4-oxo-6,7,8,9-tetra-hydro-4H-pyrido/1,2-a/-pyrimidine	3-carboxy-9-/dimethylamino-methylene/-6-methyl-4-oxo-6,7,8,9-tetra-hydro-4H-pyrido/1,2-a/-pyrimidine	59	206–208	ethanol	$C_{13}H_{17}N_3O_3$	59.30 59.19	6.51 6.52	15.96 16.10
5.	3-aminocarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-cyano-9-/dimethylamino-methylene-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/-pyrimidine	97	200–202	ethanol	$C_{13}H_{15}N_4O$	63.92 64.25	6.60 6.66	22.93 22.67
6.	3-cyano-6-methyl-4-oxo-6,7,8,9-tetra-hydro-4H-pyrido/ /1,2-a/pyrimidine	3-cyano-9-/dimethylamino-methylene-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	98	200–202	ethanol	$C_{13}H_{16}N_4O$	no melting point depression when admixed with the product of Example 5		
7.	3-ethoxyoarbonyl-4-oxo-6,7,8,9-tetra-hydro-4H-pyrido/ §1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-ethoxy-carbonyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	65	151–152	ethanol	$C_{14}H_{19}N_3O_3$	60.64 60.83	6.91 6.92	15.15 15.23

Continuation of TABLE 1

No. of Example	Starting material	Obtained product	Yield	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found C%	H%	N%
8.	6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine-3-carboxylic acid hydrazide	N^2-/dimethylamino-methylene/-9-/dimethylamino-methylene-/6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine-3-carboxylic acid hydrazide	68	177–178	ethanol	$C_{16}H_{24}N_6O_2$	57.81 57.62	7.28 7.16	25.28 25.17
9.	2-ethoxycarbonyl-1-oxo-5,6-dihydro-1H-pyrimido/1,2-a/quinoline	5-/dimethylamino-methylene/-2-ethoxycarbonyl-1-oxo-5,6-dihydro-1H-pyrimido/1,2-a/quinoline	77	172	ethanol	$C_{19}H_{19}N_3O_3$	66.45 66.85	5.89 5.68	12.91 12.82
10	3-/methylamino-carbonyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/ /1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-/methylamino-carbonyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/ /1,2-a/pyrimidine	72	210–212	ethanol	$C_{14}H_{20}N_4O_2$	60.85 61.02	7.29 7.33	20.27 20.45

EXAMPLES 11 TO 13

10.0 mmoles of a starting material given in Table 2 are dissolved in 15 ml. of dichloroethane whereafter 1.5 g. of dimethylformamide and 3.1 g. of phosphorus trichloride oxide are added at 15—20°C. The reaction mixture is stirred for 0.5 hour at room temperature, for 2 hours at 60°C, and poured to 20 g. of ice. The pH of the reaction mixture is adjusted to 6.5—7.0 by the addition of a 20% by W/V aqueous solution of sodium carbonate. The two layers are separated and the aqueous layer is shaken out with 2x 15 ml. of dichloroethane. The combined organic layer is dried with anhydrous sodium sulfate, the dichloroethane is distilled off and to the residue ether is added, the precipitated crystals are filtered, washed with ether, dried and reboiled with ether. The obtained substances and characteristic data thereof are shown in Table 2.

TABLE 2

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found		
							C%	H%	N%
11	3-ethoxycarbonyl-7-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	9-/dimethylamino-methylene/3-ethoxycarbonyl-7-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	82	152–154	ethanol-ether	$C_{15}H_{21}N_3O_3$	61.84 61.56	7.27 7.39	14.42 14.26
12	3-ethoxycarbonyl-8-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-ethoxycarbonyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido//1,2-a/pyrimidine	88	117–119	ethanol ether	$C_{15}H_{21}N_3O_3$	61.84 61.59	7.27 7.40	14.42 14.31
13	3-ethoxycarbonyl-6,8-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-ethoxycarbonyl-6,8-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	79	110	ethanol-ether	$C_{16}H_{23}N_3O_3$	62.93 62.84	7.59 7.82	13.76 13.99

EXAMPLES 14 TO 17

10.0 mmoles of a starting material given in Table 3 are dissolved in 7.3 g. of dimethylformamide and 4.3 g. of phosphorus trichloride oxide are added to the reaction mixture at 15—20°C. The reaction mixture is stirred for 0.5 hour at room temperature and for 1 hour above hot water bath. The cooled reaction mixture is poured on 30 g. of ice. The pH of the obtained solution is adjusted to 6.5—7.0 by the addition of a 20% by W/V aqueous solution of sodium carbonate. The precipitated crystals are filtered, washed with water, dried and crystallized. The obtained substances and characteristic data thereof are shown in Table 3.

TABLE 3

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found		
							C%	H%	N%
14	6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-formyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	70	178–179	ethanol	$C_{13}H_{17}N_3O_2$	63.14 63.16	6.93 7.00	16.99 16.91
15	2,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-formyl-2,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	40	176	ethanol	$C_{14}H_{19}N_3O_2$	64.35 64.18	7.33 7.66	16.08 16.00
16[x]	2-methoxy-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-formyl-2-chlor-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	69	215–216	ethanol	$C_{12}H_{14}N_3O_2Cl$	53.84 53.92 Cl% 13.24 13.58	5.27 5.58	15.70 15.54
17	3-/methylamino-carbonyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-/1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-/(N-formyl-methylamino/-carbonyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-/1,2-a/pyrimidine	85	230–232	ethanol	$C_{15}H_{20}N_4O_3$	59.20 59.43	6.62 6.97	18.41 18.46

x = In Example 16 6.1 g. of phosphorus trichloride oxide is used

EXAMPLES 18 TO 21

5.0 mmoles of a starting material given in Table 4 are dissolved in 7 ml. of dichloroethane, whereafter 1.3 g. of N-methyl-formanilide and 1.5 g. of phosphorus trichloride oxide are subsequently added to the solution. The reaction mixture is stirred for 30 minutes at room temperature and for 2 hours at boiling point under reflux. The reaction mixture is poured on 10 g. of ice after cooling and the pH of the solution is adjusted to neutral by the addition of a 20% by W/V aqueous solution of sodium carbonate. The organic and aqueous layers are separated and the aqueous part is shaken out with 2x 10 ml. of chloroethane. The combined dichloroethane solutions are dried with anhydrous sodium sulfate and dichloroethane is distilled off after filtration. Through the residue alcohol is distilled and it is treated with 10 ml. of ether. The crystals are precipitated upon cooling, filtered, washed with ether and dried. The obtained products and characteristic data thereof are shown in Table 4.

TABLE 4

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found C%	H%	N%
18	3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-ethoxycarbonyl-6-methyl-9-/N-methyl-anilino-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	77	156	ethanol	$C_{20}H_{20}N_2O_3$	67.98 67.80	6.56 6.31	11.90 11.69
19	3-/ethoxycarbonyl-methyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-/ethoxycarbonyl-methyl/-6-methyl-9-/N-methyl-anilino-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	51	109	reboiling with ether	$C_{21}H_{25}N_3O_3$	68.64 67.92	6.86 6.65	11.43 11.20
20	3,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3,6-dimethyl-9-/N-methyl-anilino-methylene/-4-oxo 6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	61	140–142	reboiling with ether	$C_{15}H_{21}N_3O$	73.19 73.16	7.17 7.10	14.23 14.05
21	3-phenyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-phenyl-6-methyl-9-/N-methyl-anilino-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	75	146–147	reboiling with ether	$C_{22}H_{23}N_3O$	77.08 76.89	6.49 6.44	11.76 11.62

EXAMPLES 22 TO 29

10.0 mmoles of a starting material as given in Table 5 are dissolved in 7.3 g. dimethylformamide and 3.1 g. of phosphorus trichloride oxide are added to the reaction mixture at 15—20°C. The reaction mixture is stirred for 1 hour at room temperature, for 1 hour at 55—60°C and for 30 minutes at 90°C. The obtained 9-[/dimethyl-iminio/-methyl]-4-oxo-6,7,8,9-tetrahydro-5H-pyrido/1,2-a/pyrimidine salt is hydrolysed without isolation to 9-formyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine by pouring the reaction mixture cooled to room temperature on ice and adjusting the pH of the reaction mixture to 6—6.5 by the addition of a 20% by W/V aqueous solution of sodium carbonate. The precipitated crystals are filtered, washed with water and dried and crystallized from the given solvent. The obtained products and data thereof are to be found in Table 5.

TABLE 5

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found C%	H%	N%
22	3-/ethoxycarbonylmethyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-/ethoxycarbonylmethyl/-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	88	109	ethanol	$C_{14}H_{18}N_2O_4$	60.42	6.52	10.07
							60.21	6.51	10.11
23	3-/ethoxycarbonylmethyl/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-/ethoxycarbonylmethyl/-9-formyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	72	162	ethanol	$C_{13}H_{16}N_2O_4$	59.08	6.10	10.60
							58.88	5.92	10.55
24	3-/ethoxycarbonylmethyl/-8-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-/ethoxycarbonylmethyl/-9-formyl-8-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/-pyrimidine	68	102	ethanol	$C_{14}H_{18}N_2O_4$	60.42	6.52	10.67
							59.98	6.36	9.94
25	3-/ethoxycarbonylmethyl/-7-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-/ethoxycarbonylmethyl/-9-formyl-7-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	85	145	ethanol	$C_{14}H_{18}N_2O_4$	60.42	6.52	10.07
							60.16	6.39	10.05
26	3,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-formyl-3,6-dimethyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	88	130	ethanol	$C_{11}H_{14}N_2O_2$	64.06	6.84	13.58
							63.86	6.99	13.60
27	3-phenyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-phenyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	86	106–108	ethanol	$C_{16}H_{16}N_2O_3$	71.62	6.01	10.44
							71.82	6.11	10.05

Continuation of TABLE 5

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found C%	H%	N%
28	3-/2',4'-dinitro-phenyl/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-/2',4'-dinitro-phenyl/-9-formyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	84	264–260	acetonitrile	$C_{15}H_{12}N_4O_6$	52.33 52.22	3.51 3.55	16.27 16.32
29	2,3-trimethylene-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/-pyrimidine	2,3-trimethylene-6-methyl-9-formyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	29	107–109	ethanol	$C_{13}H_{16}N_2O_2$	67.22 67.31	6.94 7.04	12.06 12.12

EXAMPLE 30

10.0 mmoles of 6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 7.3 g. of dimethylformamide and 1.55 g. phosphorus trichloride oxide are added dropwise at 15—20°C. The reaction mixture is then allowed to stand for 24 hours at room temperature. The obtained 9-[/dimethyl-iminio/-methyl]-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/ pyrimidine salt is hydrolysed to 9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine without isolation by pouring it on 30 g. of ice and the pH of the solution is adjusted to 6—6.5 by the addition of a 20% by W/V aqueous solution of sodium carbonate. 0.96 g. of the product is obtained. The mother liquor is shaken out twice with 10 ml. of benzene. The combined extract is dried with anhydrous benzene. The combined benzene extract is dried with anhydrous sodium sulfate, the solvent is distilled off and ethanol is distilled through the residue. A further 0.44 g. is obtained (total yield: 73%).

Analysis for the formula $C_{10}H_{12}N_2O_2$

calculated:	C 62.49%;	H 6.30%;	N 14.57%;
found:	C 62.74%;	H 6.41%;	N 14.51%;

EXAMPLES 31 TO 33

10.0 mmoles of the starting material as given in Table 6 are dissolved in 7.3 g. dimethylformamide and 3.1 g. of phosphorus trichloride oxide is added to the reaction mixture. The reaction mixture is stirred for 1 hour at room temperature, for 1 hour at 55—60°C and for 30 minutes at 90°C. The formed 9-[/-dimethyl-iminio/-methyl]-/4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine salt is converted to 9-ethoxy-methylene-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine without isolation by decomposing the reaction mixture with ethanol the water from which is removed by 20 ml. of magnesium ethylate and the reaction mixture is stirred for 1 hour at 80°C, poured to 100 ml. of water and the pH of the solution is adjusted to neutral by the addition of a 20% by W/V solution sodium carbonate. The precipitated crystals are filtered, washed with water, dried and recrystallized from the given solvent. The obtained substances and data thereof are shown in Table 6.

EXAMPLE 34

10 g. of 3-ethoxycarbonyl-6-methyl-9[/dimethyl-iminio/-methyl]-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine chloride are dissolved in 80 ml. of water and stirred for 3 hours at 60°C. The precipitated crystals are filtered, washed with water and dried. 7.4 g. (93%) of 9-formyl-3-ethoxycarbonyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are obtained. Melting point after recrystallization from ethanol: 130—132°C.

Analysis for the formula $C_{13}H_{16}N_2O_4$

calculated:	C 59.02%;	H 10.61%;	N 6.06%;
found:	C 58.87%;	H 10.53%;	N 6.26%;

TABLE 6

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found C%	H%	N%
31	6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-ethoxymethylene-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/-pyrimidine	62	62–4	ethanol	$C_{12}H_{16}N_2O_2$	65.43 65.24	7.32 7.39	12.72 12.64
32	6-methyl-3-phenyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-ethoxymethylene-6-methyl-3-phenyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido-/1,2-a/pyrimidine	87	118	ethanol	$C_{18}H_{20}N_2O_2$	72.95 72.59	6.80 6.79	9.45 9.30
33	3,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-ethoxymethylene-3,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	64	100–102	ethanol	$C_{13}H_{18}N_2O_4$	66.64 66.84	7.44 7.41	11.96 11.80

EXAMPLES 35 TO 46

10.0 mmoles of a starting material given in Table 7 are dissolved in 20 ml. of 0.5 N hydrochloric acid solution and the solution is stirred for an hour at room temperature and for 1 hour at 50°C. The reaction mixture is cooled to room temperature and the precipitated crystals are filtered, washed with water, dried and recrystallized. The obtained substances and characteristic data thereof are shown in Table 7.

TABLE 7

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found C%	H%	N%
35	9-/dimethylamino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine-3-carboxylic acid	9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidin-3-carboxylic acid	95	185–186	ethanol	$C_{11}H_{12}N_2O_4$	55.93 55.98	5.12 5.25	11.86 11.85
36	9-/dimethylamino-methylene/-3-ethoxy-carbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	83	135–136	ethanol	$C_{13}H_{16}N_2O_4$	59.08 58.64	6.10 6.25	10.60 10.67
37	9-/dimethylamino-methylene/-3-ethoxycarbonyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-ethoxycarbonyl-9-formyl/-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	83	160–161	ethanol	$C_{13}H_{14}N_2O_4$	57.59 57.51	5.64 5.86	11.19 11.13
38	9-/dimethylamino-methylene/-3-ethoxycarbonyl-8-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-ethoxycarbonyl-9-formyl-8-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	86	133	ethanol	$C_{13}H_{16}N_2O_4$	59.08 58.77	6.10 6.13	10.60 10.53
39	9-/dimethylamino-methylene/-3-ethoxycarbonyl-6,8-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-ethoxycarbonyl-9-formyl-6,8-dimethyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/-pyrimidine	92	135	ethanol	$C_{14}H_{18}N_2O_4$	60.42 60.45	6.52 6.38	10.07 9.99
40	3-cyano-9-/dimethylamino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/-pyrimidine	3-cyano-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	90	192–193	ethanol	$C_{11}H_{11}N_3O_2$	60.82 60.94	5.10 5.18	19.34 19.23

Continuation of TABLE 7

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated / found C%	H%	N%
41	9-/dimethylamino-methylene/-3-formyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3,9-diformyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	97	183	ethanol	$C_{11}H_{12}N_2O_3$	59.99 60.01	5.49 5.53	12.72 12.72
42	9-/dimethylamino-methylene/3-formyl-2,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3,9-diformyl-2,6-dimethyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	85	135	ethanol	$C_{12}H_{14}N_2O_3$	61.53 61.78	6.02 6.18	11.96 11.71
43	9-/dimethylamino-methylene/-3-ethoxycarbonyl-7-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-ethoxycarbonyl-9-formyl-7-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	85	122	ethanol	$C_{13}H_{16}N_2O_4$	59.08 58.92	6.10 6.27	10.60 10.76
44	9-/dimethylamino-methylene/-3-/methyl-amino-carbonyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-formyl-3-/methyl-amino-carbonyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	98	215–216	ethanol	$C_{12}H_{15}N_3O_3$	57.82 58.03	6.07 6.12	16.86 16.90
45	5-/dimethylamino-methylene/-2-ethoxycarbonyl-1-oxo-5,6-di-hydro-1H-pyrimido/-1,2-a/quinoline	2-ethoxycarbonyl-5-formyl-1-oxo-4,6-dihydro-1H-pyrimido/-1,2-a/quinoline	84	143–145	ethanol	$C_{16}H_{14}N_2O_4$	64.42 64.22	4.73 4.67	9.39 9.47
46	9-/dimethylamino-methylene/-3-formyl-2-chloro-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	3,9-diformyl-2-chloro-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/-pyrimidine	92	231–232	ethanol	$C_{10}H_9N_2O_3Cl$	49.91 50.24 Cl 14.73 14.97	3.77 3.80	11.64 11.62

EXAMPLE 47

To a mixture of 5.0 mmoles of 3-phenyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 1.77 g. of N,N-diethylbenzamide 1.5 g. of phosphorus trichloride oxide are added at 15—20°C. The reaction mixture is stirred for 0.5 hour at 50°C, and for 1 hour at 90°C. The formed 9-[/diethyl-iminio/-phenyl-methyl]-3-phenyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine salt is hydrolysed without isolation by adding 15 g. of icy water to the cooled reaction mixture and the mixture is stirred for 0.5 hour. The precipitated crystals are filtered, washed with water and dried. 0.6 g. (34.8%) of 9-benzoyl-3-phenyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained and recrystallized from ethanol to give a product melting at 214°C.

Analysis for the formula $C_{22}H_{20}N_2O_2$

calculated: C 76.72%; H 5.85%; N 8.13%;
found: C 76.41%; H 5.83%; N 8.25%;

EXAMPLE 48

10.0 mmoles of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 3.54 g. of N,N-diethylbenzamide are mixed together and to this mixture 3.1 g. of phosphorus trichloride oxide is added at 15—20°C. The reaction mixture is stirred for 30 minutes at 50°C, and for 1 hour at 90°C. The formed 9-[/diethyl-iminio/-phenyl-methyl]-3-ethoxycarbonyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine salt is converted to 9-[/diethylamino/-phenylmethylene]-3-ethoxycarbonyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine without isolation by pouring the cooled reaction mixture to 30 g. of ice. The acidic reaction mixture is shaken out with 3×15 ml. of ether. The aqueous solution is neutralized with a 20% by W/V solution of sodium carbonate and shaken out with 3×30 ml. of benzene. The combined benzene solution is dried with anhydrous sodium sulfate, and the benzene is distilled off. The residual oil is stirred for 1 hour with 10 ml. of 0.5 N hydrochloric acid solution at room temperature and for 1 hour at 50°C. The precipitated crystals are distilled off after cooling, washed with water, dried. 1.25 g. (36.8%) of 9-benzoyl-3-ethoxycarbonyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol melts at 166—167°C.

Analysis for the formula $C_{19}H_{20}N_2O_4$

calculated: C 67.05%; H 5.92%; N 8.23%;
found: C 67.24%; H 5.92%; N 8.18%;

EXAMPLES 49 TO 55

10.0 mmoles of a starting material as given in Table 8 are stirred with 10.0 mmoles on amine component in 25 ml. of ethanol for 3 hours at 80°C, whereafter the reaction mixture is poured on water. The precipitated crystals are filtered after cooling, washed with water, dried and recrystallized from ethanol. The obtained substances and characteristic data thereof are shown in Table 8.

TABLE 8

No. of Example	Starting material	Obtained product	Amine component	Yield %	m.p. °C	Empirical formula	Elementary analysis calculated / found C%	H%	N%
49	3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	3-ethoxycarbonyl-9-/(phenylamino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	aniline	95	174–175	$C_{19}H_{21}N_3O_5$	67.12 67.04	6.19 6.23	12.40 12.26
50	3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	3-ethoxycarbonyl-9-/(4-nitrophenyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2/-pyrimidine	4-nitro-aniline	77	217–219	$C_{19}H_{20}N_4O_5$	59.37 59.05	5.22 5.32	14.58 14.69
51	3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	3-ethoxycarbonyl-9-/(4-methylphenyl-aminomethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	4-methyl-phenyl	80	116–118	$C_{20}H_{23}N_3O_3$	67.91 67.52	6.51 6.48	11.90 11.41
52	3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido-/1,2-a/pyrimidine	3-ethoxycarbonyl-9-/(4-chlorophenyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	4-chloro-aniline	92	182–186	$C_{19}H_{20}N_3O_5Cl$	61.05 61.21	5.36 5.38	11.25 10.99
53	3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	3-ethoxycarbonyl-9-/(2-methoxycarbonyl-phenyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro/1,2-a/pyrimidine	2-methoxy-carbonyl-aniline	86	162–164	$C_{21}H_{23}N_3O_5$	63.47 63.59	5.79 5.89	10.53 10.45

TABLE 8 (Continued)

No. of Example	Starting material	Obtained product	Amine component	Yield %	m.p. °C	Empirical formula	Elementary analysis calculated / found C%	H%	N%
54	3-phenyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1.2-a/pyrimidine	3-phenyl-9-/(phenyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	aniline	84	82—84	$C_{22}H_{21}N_3O$	76.94 76.75	6.16 6.29	12.24 12.07
55	9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-/(phenylamino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	aniline	62	139—141	$C_{16}H_{17}N_3O$	71.89 71.68	6.41 6.29	15.72 15.52

EXAMPLE 56

10.0 mmoles of 3-/ethoxycarbonyl-methyl/-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are stirred with 10.0 mmoles of aniline in 25 ml. of ethanol for 3 hours at 80°C. 15 ml. of ethanol are distilled off and 1.5 ml. of a 10% by W/V solution of hydrochloric acid in ethanol is added and the mixture is cooled. The precipitated yellow crystals are filtered, washed with ethanol and dried. 3 g. (77%) of 3-/ethoxycarbonyl-methyl/-9-[/-phenyl-iminio/-methyl]-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine chloride are obtained, which after recrystallization from ethanol melts at 218°C.

Analysis for the formula $C_{20}H_{24}N_3O_3Cl$

calculated:	C 61.61%;	H 6.21%;	N 10.78%;	Cl 9.09%;
found:	C 61.89%;	H 6.24%;	N 10.63%;	Cl 8.96%;

EXAMPLES 57—62

10.0 mmoles of 3-ethoxycarbonyl-9-/(dimethyl-iminio)-methyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine chloride are stirred with 10.0 mmoles of an amine component dissolved in 25 ml. of ethanol for 3 hours at 80°C, whereafter the reaction mixture is poured on water. The precipitated yellow product is filtered, washed with water, dried and recrystallized from ethanol. The obtained products and data thereof are shown in Table 9.

TABLE 9

No. of Example	Obtained product	Used amine component	Yield %	m.p. °C	Empirical formula	Elementary analysis calculated / found C%	H%	N%
57	3-ethoxycarbonyl-9-/(phenyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/-pyrimidine	aniline	91	173–174	$C_{19}H_{21}N_3O_3$	no melting point depression when admixed with the product of Example 49		
58	3-ethoxycarbonyl-9-/(4-nitro-phenyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/-pyrimidine	4-nitroaniline	61	218–219	$C_{19}H_{20}N_4O_5$	no melting point depression when admixed with the product of Example 50		
59	3-ethoxycarbonyl-9-/(4-methyl-phenyl-amino)-methylene-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	4-methylaniline	85	116–117	$C_{20}H_{23}N_3O_3$	no melting point depression when admixed with the product of Example 51		
60	3-ethoxycarbonyl-9-/(4-chloro-phenyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	4-chloroaniline	90	184–186	$C_{19}H_{20}N_3O_3Cl$	no melting point depression when admixed with the product of Example 52		
61	3-ethoxycarbonyl-9-/(2-methoxycarbonyl-phenyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	2-methoxycarbonyl-aniline	85	162–164	$C_{21}H_{23}N_3O_5$	no melting point depression when admixed with the product of Example 53		
62	3-ethoxycarbonyl-9-/(amino-thiocarbonyl-amino)-imino-methylene/-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine	thiosemicarbazide	88	196–197	$C_{14}H_{19}N_5O_3S$	51.38 50.95	5.64 5.38	20.77 20.51

EXAMPLE 63

5.0 mmoles of 9-/dimethylamino-methylene/-3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.47 g. of aniline are allowed to stand in 10 ml. of 99.5% acetic acid for 24 hours at room temperature and poured to 450 ml. of chloroform. The solution is neutralized by 20% by W/V aqueous solution of sodium carbonate. The organic and aqueous layers are separated. The chloroform layer is dried with anhydrous sodium sulfate, followed by the removal of chloroform by distillation and through the residual oil ethanol is distilled. The mixture is cooled and it crystallizes upon cooling. 1.4 g. /82.5%/ of 3-ethoxycarbonyl-9-[/phenylamino/-methylene]-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are obtained, and crystallized from ethanol and the product does not give any melting point depression when admixed with the products of Examples 49 or 57.

EXAMPLE 64

5.0 mmoles of 3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.47 g. of aniline are allowed to stand in 10 ml. of 99.5% acetic acid for 24 hours at room temperature and the mixture is poured to 50 ml. of chloroform. The solution is neutralized with a 20% by W/V aqueous solution of sodium carbonate. The organic and aqueous layers are separated. The organic layer is dried above anhydrous sodium sulfate, the chloroform is distilled off. The residue is cooled and the product crystallizes upon cooling. 1.4 g. (82.5%) of 3-ethoxy-carbonyl-9-[/phenyl-amino/-methylene]-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give melting point depression when admixed with the product of Examples 49, 57 or 63.

EXAMPLE 65

According to Example 64 from 3-phenyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine and aniline 3-phenyl-9-[/phenyl-amino/-methylene]-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which does not give melting point depression when admixed with the product of Example 54. Yield: 87.2%.

EXAMPLE 66

According to Example 64 from 9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyridine and from aniline 9-[/phenyl-amino/-methylene]-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which does not give melting point depression when admixed with the product of Example 55. Yield: 68.2%.

EXAMPLE 67

5.0 mmoles of 9-/diethylamino-methylene/-3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are heated under reflux in 15 ml. of ethanol with 0.43 g. of piperidine for 3 hours. The reaction mixture is cooled and poured on 50 ml. of water. The precipitated yellow product is filtered, covered with water and dried. 1.16 g. (70.2%) of 3-ethoxycarbonyl-9-/piperidino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyridine is obtained, which after recrystallization from ethanol melts at 136—137°C.

Analysis for the formula $C_{18}H_{25}N_3O_3$

calculated:	C 65.24%;	H 7.64%;	N 12.68%;
found:	C 65.15%;	H 7.74%;	N 12.40%;

EXAMPLE 68

5.0 mmoles of 3-cyano-9-/dimethylamino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are stirred for 0.5 hour under reflux with 0.52 g. of hydroxyl amine in 15 ml. of ethanol. The yellow crystals precipitated from the cooled mixture are filtered and dried. 1 g. (86.2%) of 3-cyano-9-/hydroxy-aminomethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization from ethanol melts at 203°C.

Analysis for the formula $C_{11}H_{12}N_4O_2$

calculated:	C 56.89%;	H 5.21%;	N 24.12%;
found:	C 56.55%;	H 5.12%;	N 23.95%;

EXAMPLE 69

10.0 mmoles of 3-phenyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are stirred with 0.82 g. of hydroxylamine-hydrochloride in 20 ml. of ethanol for 1 hour at 60°C. The reaction mixture is cooled, the precipitated crystals are filtered, washed with ethanol and dried. 2.8 g. (87.7%) of 3-phenyl-9-/(hydroxy-imino)-methyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine hydrochloride is obtained, which after recrystallization from ethanol melts at 204°C.

Analysis for the formula $C_{15}H_{17}N_3O_2Cl$

calculated:	C 60.09%;	H 5.67%;	N 13.14%;	Cl 11.09%;
found:	C 60.40%;	H 5.56%;	N 12.94%;	Cl 11.24%;

EXAMPLE 70

According to Example 69 from 9-formyl-3,6-dimethyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine and from hydroxylamine hydrochloride salt 9-/(hydroxy-imino)-methyl/-3,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine hydrochloride is obtained which after recrystallization from ethanol melts at 205°C.

Yield: 78.1%.

Analysis for the formula $C_{11}H_{16}N_3O_2Cl$

calculated: C 51.27%; H 6.26%; N 16.30%; Cl 13.76%;
found: C 50.98%; H 6.27%; N 16.16%; Cl 13.68%;

EXAMPLE 71

5.0 mmoles of 3-/ethoxycarbonyl-methyl/-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 10 ml. of 96% ethanol at 40°C. To the solution 0.42 g. of hydroxylamine hydrochloride salt dissolved in 5 ml. of water is added. The reaction mixture is allowed to stand for 24 hours at room temperature. The solution is then neutralized with a 10% by W/V aqueous solution of sodium carbonate. The crystals precipitated upon cooling are filtered and washed with water. 3-/ethoxy-carbonyl-methyl/-9-/hydroxy-imino/-methyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from 96% ethanol melts at 150—151°C.

Analysis for the formula $C_{14}H_{19}N_3O_4$

calculated: C 57.32%; H 6.53%; N 14.33%;
found: C 57.79%; H 5.58%; N 14.14%;

EXAMPLE 72

5.0 mmoles of 3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are suspended in 8 ml. benzene dried above sodium whereafter 2.4 g. thionylchloride diluted with 2 ml. of benzene are added dropwise to the reaction mixture. The reaction mixture is then stirred at room temperature for 1 hour. The precipitated crystals are filtered, washed with benzene, dried in exsiccator. 1.3 g (83%) of 3-ethoxycarbonyl-9-chloromethylene-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine hydrochloride is obtained, which after recrystallization from a mixture of ethylacetate and ethanol melts at 157—158°C.

Analysis for the formula $C_{13}H_{16}N_2O_3Cl_2$

calculated: C 48.92%; H 5.05%; N 8.78%; Cl 22.21%;
found: C 49.24%; H 5.30%; N 8.76%; Cl 21.90%;

EXAMPLE 73

5.0 mmoles of 3-phenyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are suspended in 8 ml. of anhydrous benzene and 2.4 g. of thionyl chloride diluted with 2 ml. of benzene are added dropwise to the reaction mixture. The mixture is stirred at 50—55°C for 2 hours. The obtained solution is cooled and neutralized with a 10% by W/V solution of sodium carbonate. The two layers are separated and the benzene layer is dried with anhydrous sodium sulfate and evaporated. 1.2 g. /83.9%/ of 3-phenyl-9-chloro-methylene-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethyl acetate melts at 126—127°C.

Analysis for the formula $C_{16}H_{15}N_2OCl$

calculated: C 67.02%; H 5.27%; N 9.77%; Cl 12.36%;
found: C 67.02%; H 5.05%; N 9.73%; Cl 12.23%;

EXAMPLE 74

According to Example 73 from 9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine 0.68 g. (64.3%) of 9-chloromethylene-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained.

Analysis for the formula $C_{10}H_{11}N_2OCl$

calculated: C 57.02%; H 5.26%; N 13.30%; Cl 16.38%;
found: C 56.85%; H 5.11%; N 12.98%; Cl 17.21%;

EXAMPLE 75

2.18 g. of 6-methyl-2,3-/1-methyl-trimethylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 7.3 g. of dimethylformamide and 31 g. of phosphorus trichloride oxide is added dropwise to the reaction mixture under stirring at 15—20°C. The reaction mixture is stirred for 90 minutes and the formed 6-methyl-9-/dimethyl-iminio-methyl/-2,3-/1-methyl-trimethylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine chloride is converted without isolation as described below. The reaction mixture is poured to crushed ice and stirred for 15 minutes, while the 6-methyl-9-/dimethylamino-methylene/-2,3-/-1-methyl-trimethylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine gets hydrolysed. The pH of the reaction mixture is adjusted to 7 by the addition of a 20% by W/V solution of sodium carbonate. The precipitated crystals are filtered, washed with water and dried. 1.18 g. (46%) of 6-methyl-9-formyl-2,3-/1-methyl-trimethylene/-4-oxo-1,6,7,8-tetrahydro-4H-

pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol melts at 104—106°C.
Analysis for the formula $C_{14}H_{18}N_2O_2$
calculated: C 68.27%; H 7.37%; N 11.37%;
found: C 68.45%; H 7.32%; N 11.38%;

EXAMPLE 76

To the mixture of 0.95 g. of 3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 1.5 g. of N-methyl-pyrrolidone 2.3 g. phosphorus trichloride oxide is added. The reaction mixture is stirred for 0.5 hour at room temperature, for 1 hour at 60°C, and for 1 hour above hot water bath. The cooled reaction mixture is poured on 15 g. of ice and shaken out twice with 10 ml. of chloroform. The pH of the aqueous layer is neutralized with a 20% by W/V solution of sodium carbonate to 6.5 to 7. The precipitated product is filtered, washed with water and dried. 0.6 g. (44%) of 3-cyano-6-methyl-4-oxo-9-/N-methyl-2-pyrrolidene/-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization from ethyl acetate melts at 151—152°C.
Analysis for the formula $C_{15}H_{18}N_4O$
calculated: C 66.65%; H 6.70%; N 20.77%
found: C 66.20% H 6.76%; N 20.79%;

EXAMPLE 77

3.28 g. of (+)6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine $/\alpha/_D^{20} = +133°$ (c = 2, methanol) are dissolved in 14.6 g. of dimethylformamide and to the reaction mixture 3.06 g. of phosphorus trichloride oxide is added at 15—20°C. The reaction mixture is allowed to stand for 24 hours at room temperature, and poured on 60 g. finely crushed ice. The pH of the solution is adjusted to 6.5—7 by the addition of a 20% by W/V solution of sodium carbonate.

The decomposed reaction mixture is shaken out with 3×30 ml. of benzene and the combined benzene extract is dried with anhydrous sodium sulfate and the solvent is distilled off. To the residue 15 ml. of diethylether is added, the precipitated crystals are filtered, washed with diethylether and dried. The product is purified on a Kieselgel column. 1.5 g. (40%) of (+)9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point: 102—104°C $/\alpha/_D^{20} = +25°$ (c = 2, methanol).

EXAMPLE 78

11.8 g. (+)3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine [$/\alpha/_D^{20} = +122.5°$ (c = 2, ethanol)] are dissolved in 70 ml. of dichloroethane, followed by the addition of 7.3 g. of dimethylformamide and 15.3 g. of phosphorus trichloride oxide at 15—20°C. The reaction mixture is stirred for 0.5 hour at room temperature, for 2 hours at 60°C. The reaction mixture is cooled, poured to 150 g. of ice and the pH of the solution is adjusted to 6.5—7 by the addition of a 20% by W/V solution of sodium carbonate. The two layers are separated and the aqueous layer is shaken out with 2×100 ml. of dichloroethane. The combined dichloroethane solution is dried above anhydrous sodium sulfate and the solvent is distilled off and to the residue 50 ml. of diethylether is added. The precipitated crystals are filtered and washed with diethylether and dried. 11.74 g. (78%) of (—)3-ethoxy-carbonyl-9-/dimethylamino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are obtained, which after recrystallization from ethylacetate melts at 115—116°C. $/\alpha/_D^{20} = -345°$ (c = 2, methanol).

EXAMPLE 79

23.6 g. of (+)3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine $/\alpha/_D^{20} = +122.5°$ (c = 2, ethanol) are dissolved in 73 g. of dimethylformamide. To the solution 30.6 g. of phosphorus trichloride oxide are added at 15—20°C. The reaction mixture is stirred for 2 hours at room temperature. The reaction mixture is then poured on 300 g. of crushed ice and the pH of the solution is adjusted to 7 by the addition of a 20% by W/V solution of sodium carbonate. The solution is shaken out with 4 × 100 ml. of benzene and the combined benzene solutions are dried above anhydrous sodium sulfate and the benzene is removed by distillation. The residual oil is dissolved in 130 ml. of 0.5 N hydrochloric acid solution and stirred for 1 hour at room temperature and for 1 hour at 40°C. The pH of the two-layer system is adjusted to 5 by the addition of a 20% by W/V solution of sodium carbonate, followed by shaking out the mixture with 1 × 100 and 2 × 50 ml. of benzene. The combined benzene extract is dried above anhydrous sodium sulfate and benzene is removed by distillation and to the residue 40 ml. of diethylether and 10 ml. of petrolether are added. The precipitated crystals are filtered, washed with ether and dried.

17.2 g. (65%) of (+) 3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are obtained and purified by Kieselgel column chromatography, the pure product melts at 93—94°C. $/\alpha/_D^{20} = +39°$ (c = 2, methanol).

EXAMPLE 80

3.1 mmoles of 9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 30 ml. of acetic acid and 3.3 mmoles of N-methyl-aniline are then added to the solution.

The reaction mixture is allowed to stand for 34 hours at room temperature, followed by pouring it on 100 ml. of water. The pH of the solution is then adjusted to 6.5—7 by the addition of solid sodium carbonate. The precipitated crystals are then filtered by suction, washed with water and dried. The obtained solid is suspended in 50 ml. of petrolether and filtered. The obtained 7.2 g. (82%) of 9-/N-phenyl-N-methyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are recrystallized from acetone, melting point: 153—154°C.

Analysis for the formula $C_{17}H_{19}N_3O$

calculated: C 72.57%; H 6.81%; N 14.94%;
found: C 72.35%; H 6.82%; N 14.83%;

EXAMPLE 81

5.0 mmoles of 9-/N-phenyl-N-methyl-aminomethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 3.6 g. of dimethylformamide and 1.55 g. of phosphorus trichloride oxide are dropped at 15—20°C to the solution. The reaction mixture is stirred for 30 minutes at room temperature and for 1 hour above hot water bath. The cooled reaction mixture is poured on 15 g. of finely crushed ice and the pH of the solution is adjusted to 6.5—7.0 by the addition of a 20% by W/V solution of sodium carbonate. The precipitated crystals are filtered and washed with water. 0.9 g (58%) of 9-/N-phenyl-N-methyl-amino-methylene/-3-formyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization free ethano melts at 260—261°C.

Analysis for the formula $C_{18}H_{19}N_3O_2$

calculated: C 69.88%; H 6.19%; N 13.58%;
found: C 70.05%; H 6.13%; N 13.53%;

EXAMPLE 82

5.0 mmoles of 9-/dimethylamino-methylene/-3-carboxy-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 10 ml. of acetic acid and 0.47 g. of aniline is added to the solution. The reaction mixture is allowed to stand at room temperature, poured on 30 ml. of water, and the precipitated crystals are filtered, and dried. 1.4 g. (90%) of 9-/phenyl-aminomethylene/-3-carboxy-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which melts at 262°C after recrystallization from acetonitrile.

Analysis for the formula $C_{17}H_{17}N_3O_3$

calculated: C 65.58%; H 5.50%; N 13.50%;
found: C 65.52%; H 5.32%; N 13.36%;

EXAMPLE 83

5.0 mmoles of 3-ethoxycarbonyl-4-oxo-4,6,7,8-tetrahydro-pyrrolo/1,2-a/pyrimidine are dissolved in 7 ml. of dichloroethane and 0.73 g. of dimethylformamide and 1.55 g. of phosphorus trichloride oxide are added to the solution. The reaction mixture is stirred for 30 minutes at room temperature and for 1 hour at 60°C, and for 30 minutes above a hot water bath. The cooled reaction mixture is poured on 15 g. of crushed ice, and the pH of the solution is adjusted to 6.5—7 by the addition of a 20% by W/V solution of sodium carbonate. The two layers are separated. The aqueous layer is shaken out with 2×10 ml. of dichloroethane. The combined organic layer is dried above anhydrous sodium sulfate. The solvents are removed by distillation. To the residual oily substance 10 ml. of diethylether is added, the crystalline substance is filtered by suction. 0.75 g. (58%) of 8-/dimethylamino-methylene/-3-ethoxycarbonyl-4-oxo-4,6,7,8-tetrahydro-pyrrolo/1,2-a/pyrimidine is obtained.

Analysis for the formula $C_{13}H_{17}N_3O_3$

calculated: C 59.18%; H 6.37%; N 15.78%;
found: C 59.30%; H 6.50%; N 15.96%;

EXAMPLE 84

5.0 mmoles of 3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 7 ml. of dichloroethane. 1.2 g. of formanilide and 1.55 g. of phosphorus trichloride oxide are added and the reaction mixture is allowed to stand at room temperature and then decomposed by the addition of 15 g. of crushed ice and the pH is adjusted to 6.5—7 by the addition of a 20% by W/V solution of sodium carbonate. The two layers are separated. The aqueous layer is shaken out with 2×10 ml. of dichloroethane. The combined organic layer is dried above anhydrous sodium sulfate, the solvent is removed by distillation. Through the residual oily substance ethanol is distilled followed by crystallization from ethanolic diethylether. 0.85 g. (58%) of 3-cyano-9-/phenyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization from ethanol melts at 207°C.

Analysis for the formula $C_{17}H_{16}N_4O$

calculated: C 69.85%; H 5.50%; N 19.17%;
found: C 69.86%; H 5.74%; N 19.02%;

EXAMPLE 85

6.0 mmoles of 3-cyano-9-/dimethylamino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-

pyrido/1,2-a/pyrimidine are suspended in 15 ml. of acetic acid and stirred with 0.47 g. of aniline for 12 hours at room temperature, diluted with 30 ml. of water, the precipitated crystals are filtered by suction and dried. 1.3 g. (89%) of 3-cyano-9-/phenyl-aminomethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, the product does not give melting point depression when admixed with the product of Example 84.

EXAMPLES 86 TO 90

10.0 mmoles of a starting material as given in Table 10 and 1.4 g. of dimethylformamide-diethyl-acetate are heated under reflux in 20 ml. of benzene for 2 hours and the solvent is distilled off, the mixture is filtered, washed with ethanol and dried. The obtained substances and data thereof are shown in Table 10.

TABLE 10

No. of Example	Starting material	Obtained product	Yield %	m.p. °C	Recrystallization solvent	Empirical formula	Elementary analysis calculated found
86	3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-/1,2-a/pyrimidine	58	136–137	ethanol	$C_{15}H_{21}N_3O_3$	: no melting point depression when admixed with the product of Example 2
87	3-ethoxycarbonyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-/1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-ethoxycarbonyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	62	151–152	ethanol	$C_{14}H_{19}N_3O_3$	no melting point depression when admixed with the product of Example 7
88	3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-/1,2-a/pyrimidine	3-cyano-9-/dimethylamino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	74	200–202	ethanol	$C_{13}H_{16}N_4O$	no melting point depression when admixed with the product of Example 6
89	3-/methyl-aminocarbonyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/-1,2-a/pyrimidine	9-/dimethylamino-methylene/-3-/methyl-aminocarbonyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine	64	210–212	ethanol	$C_{14}H_{20}N_4O_2$	no melting point depression when admixed with the product of Example 10
90	2-ethoxycarbonyl-1-oxo-5,6-dihydro-1H-pyrimido/1,2-a/quinoline	5-/dimethylamino-methylene/-2-ethoxycarbonyl-1-oxo-5,6-dihydro-1H-pyrido/-/1,2-a/quinoline	60	172	ethanol	$C_{18}H_{19}N_3O_3$	no melting point depression when admixed with the product of Example 9

EXAMPLE 91

1.18 g. of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are boiled under reflux with 5 ml. of ethyl-orthoformate in 20 ml. of acetic acid anhydride for 10 hours. The solvent and the excess ethyl orthoformate are distilled off in vacuo of 0.5 mmHg, the residue is dissolved in 5 ml. of ethyl alcohol and poured on 15 ml. of water. The precipitated crystals are filtered by suction, washed with water and dried. 0.85 g (58%) of 3-ethoxycarbonyl-9-/ethoxy-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which is eluted with benzene on a column filled with alumina and melts at 114—116°C.

Analysis for the formula $C_{15}H_{20}N_2O_4$

calculated: C 61.63%; H 6.90%; N 9.59%;
found: C 62.00%; H 6.91%; N 9.52%;

EXAMPLE 92

0.95 g. of 3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is heated under reflux with 5 ml. of ethyl orthoformate in 20 ml. acetic acid anhydride for 10 hours. The solvent and the excess ethyl orthoformate are distilled off in vacuo of 0.5 mmHg and the residue is suspended in 10 ml. of ethanol, filtered after cooling and washed with cold ethanol and dried. 0.9 g. (74%) of 3-cyano-9-/ethoxymethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol melts at 166—167°C.

Analysis for the formula $C_{13}H_{15}N_3O_2$

calculated: C 63.66%; H 6.16%; N 17.13%;
found: C 64.03%; H 6.05%; N 16.95%;

EXAMPLE 93

0.35 g. of 3-phenyl-9-/(N-phenyl-N-methyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido-/1,2-a/pyrimidine is boiled under reflux with 5 ml. of 10% by W/V ethanol containing hydrochlorid acid. The cooled solution is poured on 5 ml. of water and the pH of the solution is adjusted to 7 by the addition of a 20% by W/V solution of sodium carbonate. The precipitated crystals are filtered, covered with water and dried. 0.2 g. (68%) of 9-/ethoxy-methylene/-3-phenyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give a melting point depression when admixed with the product of Example 32.

EXAMPLE 94

1.22 g. of 3-cyano-9-/ethoxy-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is heated for 2 hours with 0.47 g. of aniline in 15 ml. of ethanol under reflux. The crystals precipitated from the cooled solution are filtered, washed with cold ethanol and dried. 1.3 g. (89%) of 3-cyano-9-/phenyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give a melting point depression when admixed with the product of Examples 84 and 85.

EXAMPLE 95

0.93 g. of 3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are melted with 0.47 g. of aniline and 0.89 g. of ethyl-orthoformate under stirring at 100—110°C for 1 hour. 0.1 g. of aluminium(III)chloride is then added to the reaction mixture and the mixture is stirred at the temperature mentioned before for 20 minutes. After cooling 9 ml. of ethanol is added to the melt, which crystallizes. The precipitated crystals are filtered, washed with cold ethanol and dried. 1.0 g. (68%) of 3-cyano-9-/phenyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give any melting point depression when admixed with the product prepared according to Examples 84, 85 and 94.

EXAMPLE 96

0.95 g. 3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine, 0.47 g. of aniline and 0.89 g. of ethyl orthoformate are boiled under reflux in 10 ml. of ethanol for 16 hours. The cooled solution is poured on 15 ml. water. The precipitated crystalline substance is filtered by suction after cooling, covered by water and dried. 0.55 g. (38%) 3-cyano-9-/phenyl-aminomethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give melting point depression with any of the products of Examples 84, 85, 94 and 95.

EXAMPLE 97

1.18 g. of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are melted together with 0.47 g. of aniline and 0.89 g. of ethyl orthoformate at 100—110°C for 1 hour. 0.01 g. or aluminium(III)chloride is then added and the reaction mixture is stirred for further 20 minutes at the temperature mentioned above. To the cooled melt 1 ml. of ethanol and 15 ml. of diethylether is added. The precipitated crystalline substance is filtered by suction, washed with diethylether and dried. 1.1 g. (65%) of 3-ethoxycarbonyl-9-/phenyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give melting

point depression with any of the products of Examples 49, 57, 63 and 64.

EXAMPLE 98

1.18 g. of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.47 g. aniline and 0.89 g. of ethyl orthoformate are heated together under reflux in 10 ml. of ethanol for 14 hours. The cooled solution is poured to 15 ml. of water, the precipitated crystals are filtered by suction, washed with water and dried. 0.4 g. (24%) of 3-ethoxycarbonyl-9-/phenyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are obtained, which after recrystallization from ethanol does not give melting point depression when admixed with any of the products of Examples 49, 57, 63 and 97.

EXAMPLE 99

1.18 g. of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are stirred with 1.0 g. of N-phenyl-N'-phenyl-formamidine for 1 hour at 115—125°C and for 1 hour at 140—150°C. 1 ml. of ethanol and 15 ml. of diethylether are added to the reaction mixture. The precipitated crystals are filtered and washed with diethylether. 1.1 g. (65%) of 3-ethoxycarbonyl-9-/phenyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give melting point depression when admixed with any of the products obtained according to Examples 49, 57, 63, 64, 97 and 98.

EXAMPLE 100

5.2 g. of 3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 5.4 g. of N^1-/4-amino-phenylsulfonyl/-N^2-n-butylurea are dissolved in 50 ml. of ethanol and the solution is heated for 1 hour in the presence of 1—2 drops of conc. hydrochloric acid. White crystals are precipitating from the solution. The precipitated crystals are filtered, washed with ethanol and dried. 9.1 g. of 3-ethoxycarbonyl-9-/(4-)n-butyl-ureido-sulfonyl/-phenyl-amino/-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point: 196—198°C.

Analysis for the formula $C_{24}H_{31}N_5O_6S$

calculated:	C 55.85%;	H 6.02%;	N 13.57%;
found:	C 55.30%;	H 6.10%;	N 13.35%;

EXAMPLE 101

0.9 g. of 3-cyano-9-/ethoxy-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.35 g. of 2-amino-pyridine dissolved in 10 ml. of ethanol are heated under reflux for 2 hours. The reaction mixture is cooled and the precipitated crystals are filtered by suction, washed with ethanol and dried 0.9 g. (83%) of 3-cyano-9-/2-pyridyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization from acetonitrile melts at 251°C.

Analysis for the formula $C_{16}H_{15}N_5O$

calculated:	C 65.52%;	H 5.15%;	N 23.88%;
found:	C 65.20%;	H 4.99%;	H 23.76%;

EXAMPLE 102

0.89 g. of 9-/ethoxy-methylene/-3-phenyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.28 g. of aniline are heated for 1 hour at 100—110°C in a melt. The cooled reaction mixture is dissolved in 15 ml. of diethylether and 1 ml. of 10% by W/V ethanol containing hydrochloric acid is added and the mixture is cooled. The precipitated yellow crystals are filtered and washed with ethanol and dried. 1.1 g. (96%) of 3-phenyl-9-/(phenyl-imino)-methyl/-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine chloride is obtained, which after recrystallization from ethanol melts at 280°C.

Analysis for the formula $C_{22}H_{22}N_3OCl$

calculated:	C 69.56%;	H 5.57%;	N 11.06%;	Cl 9.33%;
found:	C 70.19%;	H 5.83%;	N 10.79%;	Cl 9.60%;

EXAMPLE 103

0.88 g. of 3-ethoxycarbonyl-9-/ethoxy-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is stirred in 6 ml. of 0.5 N hydrochloric acid solution for 30 minutes. The precipitated crystals are filtered and washed with water. 0.62 g. (78%) of 3-ethoxycarbonyl-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give melting point depression when admixed with a product of Example 36.

EXAMPLE 104

A mixture of 5.8 g. of 9-/dimethyl-amino-methylene/-3-ethoxycarbonyl-6-methyl-4-oxo-4H-pyrido/1,2-a/pyrimidine, 2.8 g. of glycine ester chlorohydrate and 60 ml. of methanol is heated for 12 hours and the solvents is distilled off and the obtained oil is triturated with water, and thus crystallized,

filtered, and dried. 3.1 g. (44%) of 3-ethoxycarbonyl-9-/(ethoxycarbonyl-methyl-amino)-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization from methanol melts at 155—157°C.
Analysis for the formula $C_{17}H_{23}N_3O_5$
calculated: C 58.48%; H 6.57%; N 12.05%;
found: C 58.57%; H 6.67%; N 11.62%;

EXAMPLE 105

0.95 g. of 3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is dissolved in 3.1 g. of dimethylformamide and 1.55 g. of phosphorus trichloride oxide is added to the reaction mixture at 15—20°C, and the mixture is stirred for 2 hours at room temperature. The mixture is then decomposed by 10 ml. of ethanol, dried with magnesium ethylate and boiled for 30 minutes under reflux. The decomposed reaction mixture is poured on 50 ml. of icy water, while maintaining the pH at a constant value of 7, by adding a 20% by W/V solution of sodium carbonate. The precipitated crystals are filtered and washed with water. 0.9 g. (74%) of 3-cyano-9/ethoxy-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which does not give melting point depression when admixed with the product prepared according to Example 92.

EXAMPLE 106

0.73 g. of 3-(ethoxycarbonyl-methyl)-9-(phenyl-methyl-amino-methylene)-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is heated under reflux in 8 ml. of 10% by W/V ethanol containing hydrochloric acid for 1 hour, the cooled solution is poured on 30 ml. of water and the pH is adjusted to 7 by the addition of a 20% by W/V solution of sodium carbonate. The aqueous solution is shaken out with 3x20 ml. of benzene, the combined benzene extract is dried above anhydrous sodium sulfate and the solvent is distilled off. The residual oily product is purified by Kieselgel-$PF_{254-366}$ thin layer chromatography. 0.4 g. (65%) of 3-/ethoxycarbonyl-methyl/-9-/ethoxy-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained.
Analysis for the formula $C_{16}H_{22}N_2O_4$
calculated: C 62.72%; H 7.24%; N 9.14%;
found: C 62.51%; H 7.11%; N 9.36%;

EXAMPLE 107

From 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine 3-ethoxycarbonyl-9-/ethoxy-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained according to Example 105 which does not give melting point depression when admixed with the product of the Example 91.

EXAMPLE 108

0.45 g. of 3-phenyl-9-/chloromethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.12 g. of ammonium rhodanide is stirred for 1 hour at room temperature in 6 ml. of acetone dried above potassium carbonate, and poured on 20 ml. of water. The precipitated crystalline substance is filtered by suction, washed with water and dried. 0.44 g. (93%) of 3-phenyl-6-methyl-4-oxo-9-/thiocyanatomethylene/-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization melts at 124°C.
Analysis for the formula $C_{17}H_{15}N_3OS$
calculated: C 66.00%; H 4.89%; N 13.59%; S 10.36%;
found: C 65.48%; H 4.89%; N 13.23%; S 10.24%;

EXAMPLE 109

5.0 mmoles of 3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 10 ml. of dichloroethane, whereafter 1.3 g. of N-methylformanilide and 1.5 g. of phosphorus trichloride oxide are added to the solution. The reaction mixture is stirred for 30 minutes at room temperature and further 30 minutes at the boiling point under reflux. The cooled reaction mixture is poured on 10 g. of ice and the pH is adjusted to neutral by adding a 20% by W/V solution of sodium carbonate. The aqueous and organic layers are separated and the aqueous layer is shaken out twice with 10 ml dichloroethane. The combined dichloroethane solution is dried above anhydrous sodium sulfate and dichloroethane is distilled off after filtration. Through the residue ethanol is distilled and it is recrystallized from 5 ml. of ethyl acetate and 15 ml. diethylether. The precipitated crystals are cooled, filtered and washed with ethyl acetate. 1.25 g. (82%) 3-cyano-6-methyl-9-/N-methyl-anilino-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization from ethyl acetate melts at 161—163°C.
Analysis for the formula $C_{18}H_{18}N_4O$
calculated: C 70.57%; H 5.92%; N 18.29%;
found: C 70.53%; H 6.03%; N 18.03%;

EXAMPLE 110

50 mmoles of 3-/methoxycarbonyl)-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 70 ml. dichloroethane. 7.3 g. N,N-dimethylformamide and 15.3 g. of phosphorus trichloride oxide are added and the mixture is stirred for 30 minutes at room temperature and for 60 minutes under reflux. The cooled reaction mixture is poured on 150 g. of ice and the pH is adjusted to neutral by adding 20% by W/V solution of sodium carbonate. The two layers are separated and the aqueous layer is shaken out twice with 75 ml. of dichloroethane. The combined organic layer is dried above anhydrous sodium sulfate and evaporated. Through the residue ethyl acetate is distilled and the mixture is crystallized from ethanol. 7.8 g. (70%) of 3-/methoxy-carbonyl/-6-methyl-9-/dimethylamino-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol melts at 180°C.

Analysis for the formula $C_{14}H_{19}N_3O_3$

calculated: C 60.63%; H 6.91%; N 15.17%;
found: C 60.30%; H 7.10%; N 14.96%;

EXAMPLE 111

10 mmoles of 3-/methoxycarbonyl/-6-methyl-9-/dimethyl-amino-methylene/-4-oxo/6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are stirred in 20 ml. 0.5 N hydrochloric acid for 2 hours at room temperature and for 1 hour at 50°C. The suspension is cooled to 5°C and filtered by suction, washed with water. 1.85 g. (74%) of 9-formyl-3-/methoxy-carbonyl/-6-methyl-4-oxo-1,6,7,8-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from methanol melts at 155°C.

Analysis for the formula $C_{12}H_{14}N_2O_4$

calculated: C 57.59%; H 5.64%; N 11.19%;
found: C 57.20%; H 5.51%; N 10.99%;

EXAMPLE 112

5.0 mmoles of 6,8-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine-3-carboxamide are dissolved in 3.15 g. of dimethylformamide and 1.5 g. of phosphorylchloride oxide are added dropwise at 20°C to the reaction mixture. The mixture is then stirred for 2 hours at room temperature, poured on 15 g. of ice and the pH is adjusted to neutral by adding 20% by W/V sodium carbonate solution. The precipitated substance is filtered by suction after cooling and washed with water. 1 g. (78%) of 3-cyano-6,8-dimethyl-9-/dimethyl-amino-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which melts at 133—135°C after recrystallization from ethanol.

Analysis for the formula $C_{14}H_{18}N_4O$

calculated: C 65.09%; H 7.02%; N 21.69%;
found: C 65.28%; H 7.13%; N 21.56%;

EXAMPLE 113

1.94 mmoles of 3-cyano-6,7-dimethyl-9-/dimethyl-amino-methylene/-4-oxo-4H-pyrido/1,2-a/pyrimidine are stirred in 4 ml. of 0.5 N hydrochloric acid solution for 1 hour at room temperature and for 1 hour at 50°C. The mixture is cooled, filtered, washed with water. 0.42 g. (93.8%) of 3-cyano-9-formyl-6,8-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which melts at 139—140°C after recrystallization from ethanol.

Analysis for the formula $C_{12}H_{13}N_3O_2$

calculated: C 62.33%; H 5.67%; N 18.17%;
found: C 62.13%; H 5.67%; N 18.07%;

EXAMPLE 114

5.0 mmoles of 3-cyano-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.36 g. of n-butylamine are heated in 10 ml. of ethanol under reflux for 3 hours, and the reaction mixture is then allowed to stand for 12 hours at —10°C. The precipitated crystals are filtered and washed with ethanol. 0.77 g. (57%) 9-/n-butyl-amino-methylene/-3-cyano-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization from ethyl acetate melts at 142°C.

Analysis for the formula $C_{15}H_{20}N_4O$

calculated: C 66.15%; H 7.40%; N 20.57%;
found: C 65.88%; H 7.43%; N 20.35%;

EXAMPLE 115

5.0 mmoles of 3-cyano-9-/ethoxy-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are boiled for 2 hours with 0.37 g. of diethylamine in 15 ml. of ethanol under reflux. The reaction mixture is allowed to stand for 12 hours at —10°C and the precipitated crystals are filtered by suction and washed with ethanol. 1.25 g. (91%) of 3-cyano-9-/diethylamino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which melts at 145°C after recrystallization from ethyl acetate.

Analysis for the formula $C_{15}H_{20}N_4O$
calculated: C 66.15%; H 7.40%; N 20.57%;
found: C 65.80%; H 7.53%; N 20.42%;

EXAMPLE 116

10.00 mmoles of 3-/ethoxycarbonyl-methyl/-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine are suspended in 15 ml. of anhydrous benzene and 5 ml. of thionyl chloride diluted with benzene are added dropwise to the reaction mixture. The mixture is stirred for 2 hours at 50—55°C, and cooled to 5—10°C. The precipitated 3-/ethoxymethylene-methyl/-9-/chloromethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidinium chloride is filtered, washed with anhydrous benzene. The salt is dried in vacuo above calcium chloride. The salt is then suspended in a 15-fold amount of anhydrous benzene and an equivalent amount of triethyl amine is added to the suspension. The precipitated triethylammonium chloride is filtered and the filtrate is evaporated. The residual oily product is cooled and filtered by suction. 1.81 g. (61%) of 3-/ethoxymethylene-methyl/-9-/chloromethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point: 51—53°C.
Analysis for the formula $C_{14}H_{17}ClN_2O_3$
calculated: C 56.66%; H 5.77%; N 9.44%; Cl 11.95%;
found: C 56.15%; H 5.65%; N 9.33%; Cl 11.58%;

EXAMPLE 117

From 10.0 mmoles of 9-formyl-3,6-dimethyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine 1.5 g. (67%) of 9-/chloromethylene/-3,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained according to Example 116 and the product melts at 63°C.
Analysis for the formula $C_{11}H_{13}ClN_2O$
calculated: C 58.80%; H 5.83%; N 12.47%; Cl 15.78%;
found: C 58.77%; H 5.92%; N 12.41%; Cl 15.42%;

EXAMPLE 118

0.5 g. of 3-ethoxycarbonyl-9-/chloromethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is dissolved in 5 ml. of acetone dried above potassium carbonate and 0.51 g. of ammonium rhodanide is added. The reaction mixture is stirred for 2 hours at —3°C to 5°C and poured to 20 ml. of water. The precipitated crystalline substance is filtered by suction after cooling and washed with water. 0.45 g. (83%) of 3-ethoxycarbonyl-6-methyl-4-oxo-9-/thiocyanato-methylene/-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point: 108°C.
Analysis for the formula $C_{14}H_{15}N_3O_3S$
calculated: C 55.07%; H 4.94%; N 13.76%; S 10.50%;
found: C 55.15%; H 4.89%; N 13.69%; S 10.61%;

EXAMPLE 119

5.0 mmoles of 9-/chloromethylene/-3,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are reacted with 0.46 g. of ammonium rhodanide as described in Example 118 and thus 0.92 g. (74%) 3,6-dimethyl-9-/thiocyanatomethylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point: 108°C.
Analysis for the formula $C_{12}H_{13}N_3OS$
calculated: C 58.28%; H 5.30%; N 16.99%; S 12.97%;
found: C 58.90%; H 5.58%; N 16.86%; S 12.79%;

EXAMPLE 120

According to Example 118 5.0 mmoles of 3-/ethoxycarbonyl-methyl/-9-/chloromethylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.46 g. of ammonium rhodanide are reacted and 0.97 g. (61%) 3-/ethoxycarbonyl-methyl/-6-methyl-4-oxo-9-/thiocyanato-methylene/-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point: 98°C.
Analysis for the formula $C_{15}H_{17}N_3O_3S$
calculated: C 56.41%; H 5.37%; N 13.16%; S 10.04%;
found: C 56.07%; H 5.45%; N 13.22%; S 10.05%;

EXAMPLE 121

5.0 mmoles of 3-ethyl-2,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 3.65 g. of dimethylformamide and 1.5 g. of phosphorus trichloride oxide is added at 15—20°C. The reaction mixture is then stirred for 1 hour at room temperature, for 1 hour at 55—60°C and for 30 minutes at 90°C. The formed 3-ethyl-9-/(dimethyl-imino)-methyl/-2,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine salt is hydrolysed without isolation to give 3-ethyl-9-formyl-2,6-dimethyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine by pouring the cooled reaction mixture on 15 g. of ice and the pH of the solution is adjusted to 6—6.5 by adding a 20% by W/V solution of sodium carbonate. The precipitated crystals are filtered and washed with water. 0.85 g.

(72.5%) of crystalline substance is obtained, which melts at 114—116°C after recrystallization from ethyl acetate.
Analysis for the formula $C_{13}H_{18}N_2O_2$
calculated: C 70.34%; H 6.52%; N 12.95%
found: C 69.85%; H 6.67%; N 12.08%;

EXAMPLE 123

1.5 mmoles of 7-ethoxycarbonyl-3-phenyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are heated for 1 hour under reflux with 0.22 g. of dimethylformamide and 0.46 g. phosphorus trichloride oxide in 5 ml. dichloroethane. The cooled reaction mixture is poured on 5 g. of ice and the pH is adjusted to 7 by adding a 20% by W/V solution of sodium carbonate. The two layers are separated and the aqueous layer is shaken out with 2×5 ml. of dichloroethane. The combined organic layer is dried above anhydrous sodium sulfate and the solvent is distilled off. The residual 9-/dimethylamino-methylene/-7-ethoxy-carbonyl-3-phenyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is converted without isolation by stirring it in 3 ml. of 0.5 N hydrochloric acid solution for 3 hours at room temperature. The precipitated crystalline substance is filtered, washed with water. 0.3 g. (61%) of 7-ethoxycarbonyl-3-phenyl-9-formyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point after recrystallisation from ethanol: 146°C.
Analysis for the formula $C_{18}H_{18}N_2O_4$
calculated: C 66.25%; H 5.56%; N 8.85%;
found: C 66.80%; H 5.63%; N 8.48%;

EXAMPLE 124

5.0 mmoles of 6-methyl-4-oxo-2-piperidyl-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 3.65 g. of dimethylformamide and 1.5 g. phosphorus trichloride oxide is added at 15—20°C. The reaction mixture is then stirred for 6 hours at room temperature and poured on 20 g. of ice. The pH of the solution is adjusted to 6—6.5 by adding a 20% by W/V solution of sodium carbonate. The neutral solution is shaken out with 1×50 ml. and 2×30 ml. of benzene and the combined benzene extract is dried above anhydrous sodium sulfate and the solvent is distilled off. Through the residue ethyl acetate is distilled. The oily substance is triturated with petrolether. 0.6 g. (43%) of 9-/formyl-6-methyl-4-oxo-2-piperidyl-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point after recrystallization from ethanol: 206—207°C.
Analysis for the formula $C_{15}H_{21}N_3O_2$
calculated: C 65.43%; H 7.69%; N 15.26%;
found: C 64.84%; H 7.74%; N 15.40%;

EXAMPLE 125

10.0 mmoles of 3-/ethoxycarbonyl-ethyl/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 7.3 g. of dimethylformamide and 3.1 g. of phosphorylchloride oxide is added dropwise at 20°C. The reaction mixture is then stirred for 1 hour at room temperature and for 2 hours at 60°C. The reaction mixture is cooled and poured on 30 g. of ice. The pH of the aqueous reaction mixture is adjusted to neutral by adding a 20% by W/V solution of sodium carbonate. The precipitated crystalline substance is cooled, filtered by suction and washed with water. 2.2 g. (79%) of 3-/ethoxycarbonyl-ethyl/-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, melting point after recrystallization from ethanol: 112°C.
Analysis for the formula $C_{14}H_{18}N_4O$
calculated: C 61.63%; H 6.90%; N 9.58%;
found: C 61.62%; H 7.02%; N 9.51%;

EXAMPLE 126

5.0 mmoles of 3-cyano-9-formyl-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine and 0.51 g. of phenylhydrazine are reacted according to Example 114 to give 1.25 g. (81%) of 3-cyano-9-/2'-phenyl-hydrazino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine. Melting point: 188°C (ethanol).
Analysis for the formula $C_{17}H_{18}N_5O$
calculated: C 66.22%; H 5.88%; N 22.71%;
found: C 66.40%; H 5.78%; N 22.82%;

EXAMPLE 127

10.0 mmoles of (+) 3-carboxy-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine $\alpha_D^{20} = +116°$ (c = 2, methanol) are used as starting material according to Example 112 and 1.2 g. (38%) of (—)3-carboxy-9-/-dimethyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained which after recrystallization from ethanol melts at 219°C. $\alpha_D^{20} = -497° \pm 5$ (c = 1, methanol).

EXAMPLE 128

2.1 mmoles (—)3-carboxy-9-/dimethyl-amino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine ($\alpha_D^{20} = -497° \pm 5$, c = 2, methanol) as starting material is hydrolysed according to Example 113 and 0.35 g. (71%) of (+) 9-formyl-3-carboxy-6-methyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol melts at 168—170°C. $\alpha_D^{20} = +5°$ (c = 1, methanol).

EXAMPLE 129

1.26 g. of dimethylsulfate and 0.75 g. of dimethylformamide are heated for 2 hours at 80°C. 5.0 mmoles of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is added to the thus prepared iminium salt, whereafter the reaction mixture is kept for 4 hours at 60°C. The mixture is then cooled, poured on 15 g. of ice and thus the pH of the solution is adjusted to 7 by adding a 20% by W/V solution of sodium carbonate. The aqueous solution is shaken out with 3×10 ml. of benzene, dried above sodium sulfate and the solvent is distilled off. The residual oil is purified by Kieselgel thin layer chromatography. The separated 9-/dimethylamino-methylene/-3-ethoxy-carbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine does not give melting point depression when admixed with the product of Examples 2 and 3.

EXAMPLE 130

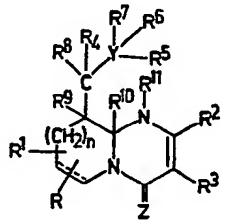
10.0 mmoles of 3-ethoxycarbonyl-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are reacted with 2.3 g. of N-formyl-piperidine and 3.1 g. of phosphorus trichloride oxide according to Example 109 and thus 3.25 g. (98%) of 3-ethoxycarbonyl-9-/piperidino-methylene/-6-methyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give melting point depression when admixed with the product of Example 67.

EXAMPLE 131

10.0 mmoles of 3,6-dimethyl-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/pyrimidine are dissolved in 20 ml. of dichloroethane and the solution is stirred together with 2.3 g. of N-formyl-piperidine and 3.1 g. of phosphoryl chloride oxide for 30 minutes at room temperature and under reflux for 1 hour. The cooled reaction mixture is poured on 20 g. of ice and the pH is adjusted to 7 by adding a 20% by W/V solution of sodium carbonate. The two layers are separated, the aqueous layer is shaken out with 2×15 ml. of dichloroethane. The combined dichloroethane solution is dried with sodium sulfate and the solvent is distilled off. The formed 3,6-dimethyl-9-/piperidino-methylene/-4-oxo-6,7,8,9-tetrahydro-4H-pyrido/1,2-a/-pyrimidine is stirred for 1 hour at room temperature in 15 ml. of 0.5 ml. of 0.5 N hydrochloric acid solution. The precipitated crystalline substance is filtered by suction and washed with water. 1.1 g. (53%) of 9-formyl-3,6-dimethyl-4-oxo-1,6,7,8-tetrahydro-4H-pyrido/1,2-a/pyrimidine is obtained, which after recrystallization from ethanol does not give melting point depression with the product of Example 26.

CLAIMS

1. Compounds of the general formula (I)



(I)

[wherein

R represents hydrogen, C_{1-4} alkyl or alkoxycarbonyl containing 1—4 carbon atoms in the alkoxy moiety;

R^1 represents hydrogen or C_{1-4} alkyl; or

R and R^1 together form $—(CH=CH)_2—$ being attached to the two adjacent ring-carbon atoms in which case the dotted line represents a carbon-carbon bond,

R^2 represents hydrogen, halogen, C_{1-4} alkyl, phenyl or a 5- or 6-membered monocyclic heterocyclic saturated ring;

R^3 represents hydrogen, optionally substituted phenyl, C_{1-4} acyl, carboxy, alkoxycarbonyl containing C_{1-6} alkoxy, nitrile, carbamoyl, alkylcarbamoyl, alkyl, C_{1-4} alkanoyl substituted carbamoyl, acid-hydrazido, (—$CONHNH_2$) or —CO—NH—N=C ($R^{12}R^{13}$) (wherein R^{12} and R^{13}, which may be the same or different, each represents C_{1-4} alkyl or carboxyalkyl or alkoxycarbonyl-alkyl or phenyl,

or

R^2 and R^3 form together $—(CH_2)_t$ (wherein t is 3 or 4),

Z represents oxygen and
n is 0, 1 or 2 and
a) if R^{11} is hydrogen and R^9 and R^{10} together and R^7 and R^8 together each form a chemical bond then
R^4 stands for hydrogen or phenyl,
Y represents an oxygen atom without its lone pairs of electrons, in which case
R^5 and R^6 each represents a lone pair of electrons or
Y represents a nitrogen atom without its lone pair of electrons and
R^5 represents C_{1-4} alkyl optionally substituted by hydroxy, carboxy or alkoxycarbonyl containing C_{1-6} alkoxy or phenyl optionally substituted by one or several nitro, C_{1-4} alkyl, or alkoxycarbonyl containing C_{1-6} alkoxy, and/or halogen; mono- or bicyclic nitrogen-containing heteroaryl, hydroxy, aminothiocarbonyl, aminothiocarbonylamino or phenylamino,
R^6 represents an unshared electron-pair, hydrogen or C_{1-4} alkyl, and in these two cases a salt is formed between the positive nitrogen and an anion, or
R^5 and R^6 together form $-(CH_2)_p$ (wherein p is 4 or 5) and a salt is formed with the positive nitrogen; or
b) if R^{10} and R^{11} together form a chemical bond and R^9 stands for hydrogen, R^8 and R^7 together form a chemical bond, then R^4, R^5, R^6 and Y are as given under item (a); or
c) if R^8 and R^9 together, and R^{10} and R^{11} together each form a chemical bond, then
R^4 represents hydrogen or phenyl, and
Y, R^5, R^6, R^7 together form a halogen atom; or
Y represents an oxygen atom without its lone pairs of electrons,
R^6 and R^7 each represents an unshared electron-pair, and
R^5 represents hydrogen or C_{1-4} alkyl; or
Y represents a sulfur atom without its lone pairs of electrons,
R^6 and R^7 each represents a lone pair of electrons, and
R^5 is cyano; or
Y represents a nitrogen atom without its lone pair of electrons,
R^5 represents C_{1-4} alkyl optionally substituted by hydroxy, carboxy, or alkoxycarbonyl or phenyl optionally substituted by nitro, C_{1-4} alkyl, or alkoxycarbonyl containing C_{1-6} alkoxy, and/or halogen; mono- or bicyclic nitrogen containing heteroaryl,
R^6 represents hydrogen or C_{1-4} alkyl, or
R^4 and R^6 together form $-(CH_2)m-$ wherein m is 3 or 4, or
R^5 and R^6 together form $-(CH_2)_p-$ wherein p is 4 or 5, and
R^7 represents an unshared pair of electrons] and the tautomers and salts thereof.

2. Compounds as claimed in claim 1, wherein n is 0.

3. Compounds as claimed in claim 1, wherein n is 1.

4. Compounds as claimed in claim 1, wherein R represents a hydrogen atom.

5. Compounds as claimed in any one of claims 1 to 3 wherein R represents an alkyl group with 1 to 4 carbon atoms.

6. Compounds as claimed in claim 5 wherein R represents a methyl group.

7. Compounds as claimed in claim 6 wherein R represents a methyl group in the 6-position.

8. Compounds as claimed in any one of the preceding claims wherein R^1 represents a hydrogen atom.

9. Compounds as claimed in any one of claims 1 to 7 wherein R^1 represents an alkyl group with 1 to 4 carbon atoms.

10. Compounds as claimed in claim 9 wherein R^1 represents a methyl group.

11. Compounds as claimed in any one of the preceding claims wherein R^2 represents hydrogen, halogen, phenyl or a 5- or 6-membered saturated monocyclic heterocyclic ring.

12. Compounds as claimed in any one of the preceding claims in which R^{11} represents a hydrogen atom, R^9 and R^{10} together form a carbon-carbon bond, R^7 and R^8 together form a carbon-nitrogen bond, R^4 represents hydrogen or phenyl and Y represents a nitrogen atom wihout its lone pair of electrons wherein R^5 represents pyridyl, hydroxy, aminothiocarbonyl, aminothiocarbonylamino or phenylamino.

13. Compounds as claimed in any one of claims 1 to 11 in which R^9 represents a hydrogen atom, R^{10} and R^{11} together form a carbon-carbon bond, R^7 and R^8 together form a carbon-nitrogen bond, R^4 represents hydrogen or phenyl and Y represents a nitrogen atom without its lone pair of electrons wherein R^5 represents pyridyl, hydroxy, aminothiocarbonyl, aminothiocarbonylamino or phenylamino.

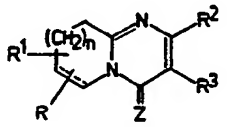
14. Compounds as claimed in any one of claims 1 to 11 in which R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, R^7 represents a lone pair of electrons and Y represents a nitrogen without its lone pair of electrons wherein R^5 represents pyridyl, hydroxy, aminothiocarbonyl, aminothiocarbonylamino or phenylamino.

15. Compounds as claimed in any one of the preceding claims in the form of their physiologically compatible salts.

16. Compounds as claimed in any one of the preceding claims in the form of their optically active isomers.

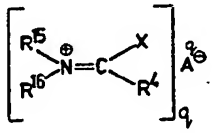
17. Compounds as claimed in claim 1 as herein specifically disclosed.

18. A process for the preparation of compounds as claimed in claim 1 [wherein R^9 represents hydrogen, R^{10} and R^{11} together form a carbon-carbon bond, R^7 and R^8 together form a carbon-nitrogen bond, Y represents a nitrogen atom, R^5 represents the radical R^{15} which represents alkyl optionally substituted by hydroxy, carboxy or alkoxycarbonyl in which the alkoxy moiety contains from 1 to 6 carbon atoms, phenyl optionally substituted by at least one nitro, C_{1-4} alkyl or alkoxycarbonyl in which the alkoxy moiety contains from 1 to 6 carbon atoms, and/or halogen; mono- or bi-cyclic nitrogen containing heteroaryl and R^6 represents the radical R^{16} which represents hydrogen or C_{1-4} alkyl or R^4 and R^5 together form a group $—(CH_2)_m—$ (wherein m is as defined in claim 1) or R^5 and R^6 together form a group $—(CH_2)_p—$ (wherein p is as defined in claim 1)] or a tautomer thereof, which process comprises reacting a compound of the formula:



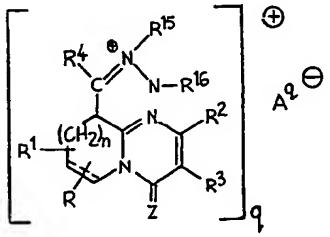
(II)

(wherein R, R^1, R^2, R^3, z and n as defined in claim 1) with a compound of the general formula



(III)

wherein R^4 represents hydrogen or phenyl, R^{15} and R^{16} are as herein defined or R^4 and R^{16} together form a group $—(CH_2)_m—$ (wherein m is as herein defined) or R^{15} and R^{16} together form a group $—(CH_2)_p—$ (wherein p is as herein defined), X represents a leaving atom or group, A represents an anion and q is the charge on the anion] whereby a compound of the formula



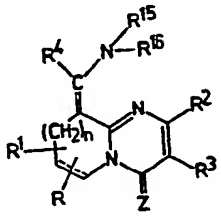
(Ia)

(wherein R, R^1, R^2, R^3, R^4, R^{15}, R^{16}, A, Z, n and q are as herein defined) or a tautomer or salt thereof is obtained.

19. A process as claimed in claim 18 wherein a compound of formula III is used in which X represents a halogen atom or a C_{1-4} alkoxy group.

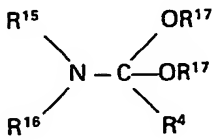
20. A process as claimed in claim 18 or claim 19 wherein a compound of formula III is used in which R^{15} represents a pyridyl group.

21. A process for the preparation of compounds as claimed in claim 1 having the formula:



(Ib)

(wherein R, R^1, R^2, R^3, R^4, Z and n are as defined in claim 1 and R^4, R^{15} and R^{16} are as defined in claim 18) or a tautomer thereof, which process comprises reacting a compound of formula II (as defined in claim 18) with a compound of the formula:—

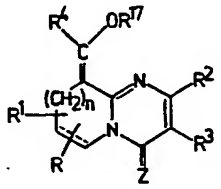


(wherein R^4, R^{15} and R^{16} are as defined in claim 18 and R^{17} represents an alkyl group) whereby a compound of formula Ib or a tautomer or salt thereof as herein defined is obtained.

22. A process as claimed in claim 21 wherein a compound of formula IV is used in which R^{17} represents a C_{1-4} alkyl group.

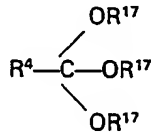
23. A process as claimed in claim 21 or claim 22 wherein R^{15} represents a pyridyl group.

24. A process for the preparation of compounds as claimed in claim 1 having the formula:—



(Ic)

(wherein R, R^1, R^2, R^3, R^4, Z and n are as defined in claim 1 and R^{17} is as defined in claim 21) or a tautomer thereof, which process comprises reacting a compound of formula II as defined in claim 18 with a compound of the formula:

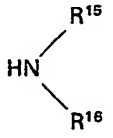


(V)

(wherein R^4 is as defined in claim 18 and R^{17} is as defined in claim 21) whereby a compound of formula Ic as herein defined or a tautomer or salt thereof is obtained.

25. A process as claimed in claim 24 wherein a compound of formula V is used in which R^{17} represents a C_{1-4} alkyl group.

26. A process for the preparation of compounds of formula Ib as defined in claim 21 or a tautomer or salt thereof which comprises reacting a compound of formula II as defined in claim 18 with a compound of the formula



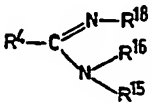
(VI)

(wherein R^{15} and R^{16} are as defined in claim 18) and with a compound of formula V as defined in claim 24 whereby a compound of formula Ib as defined in claim 21 or a tautomer or salt thereof is obtained.

27. A process as claimed in claim 26 wherein a compound of formula V is used in which R^{17} represents a C_{1-4} alkyl group.

28. A process as claimed in claim 26 or claim 27 wherein a compound of formula VI is used in which R^{15} represents a pyridyl group.

29. A process for the preparation of compounds of formula IB as defined in claim 21 or a tautomer or salt thereof which comprises reacting a compound of formula II as defined in claim 18 with a compound of the formula:—



(VII)

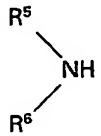
(wherein R^4, R^{15} and R^{16} are as defined in claim 18 and R^{18} represents a phenyl group) whereby a compound of formula Ib as defined in claim 21 or a tautomer or salt thereof is obtained.

30. A process for the preparation of compounds as claimed in claim 1 (wherein R^{11} represents hydrogen, R^9 and R^{10} together form a carbon-carbon bond, Y, R^5 and R^6 together represent an oxygen atom R^7 and R^8 together form a carbon-oxygen bond and R^4 represents hydrogen or phenyl) or a tautomer thereof which process comprises hydrolysing a compound of formula I as defined in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents a lone pair of electrons, R^6 represents C_{1-4} alkyl, R^5 represents C_{1-4} alkyl or optionally substituted phenyl and R^{10} and R^{11} together form a carbon-carbon bond) or a tautomer thereof whereby a compound as claimed in claim 1 (wherein R^{11}

represents hydrogen, R^9 and R^{10} together form a carbon-carbon bond, Y, R^5 and R^6 together represent an oxygen atom R^7 and R^8 together from a carbon-oxygen bond and R^4 represents hydrogen or phenyl) or a tautomer thereof is obtained.

31. A process for the preparation of compounds as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents an oxygen atom without its lone pairs of electrons, R^7 and R^6 each represent a lone pair of electrons and R^5 represents C_{1-4} alkyl) or a tautomer thereof which process comprises treating a compound as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents a lone pair of electrons, R^6 represents C_{1-4} alkyl, R^5 represents C_{1-4} alkyl or optionally substituted phenyl and R^{10} and R^{11} together form a carbon-carbon bond) or a tautomer thereof whereby a compound as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents an oxygen atom without its lone pairs of electrons, R^7 and R^6 each represent a lone pair of electrons and R^5 represents C_{1-4} alkyl) or a tautomer thereof is obtained.

32. A process for the preparation of compounds as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons and R^7 represents a lone pair of electrons) or a tautomer thereof, which process comprises reacting a compound as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents a lone pair of electrons, R^6 represents C_{1-4} alkyl, R^5 represents C_{1-4} alkyl or optionally substituted phenyl and R^{10} and R^{11} together form a carbon-carbon bond) or a tautomer thereof with an amine of the formula:



(VIII)

(wherein R^5 and R^6 are as defined in claim 1) whereby a compound as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons and R^7 represents a lone pair of electrons) or a tautomer thereof is obtained.

33. A process as claimed in claim 32 wherein the compound of formula I is used in the form of its hydrochloride salt.

34. A process as claimed in claim 32 or claim 33 wherein the reaction is effected in the presence of an alkane carboxylic acid.

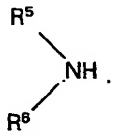
35. A process for the preparation of compounds as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons and R^7 represents a lone pair of electrons) or a tautomer thereof, which process comprises a compound as claimed in claim 1 (wherein R^7 and R^8 together form a carbon-oxygen bond, R^9 and R^{10} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, R^{11} represents hydrogen and Y, R^5 and R^6 together represent an oxygen atom) or a tautomer thereof with an amine of formula VIII as defined in claim 32 whereby a compound as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons and R^7 represents a lone pair of electrons) or a tautomer thereof is obtained.

36. A process for the preparation of compounds as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond and Y, R^5, R^6 and R^7 together represent a halogen atom) or a tautomer thereof which process comprises reacting a compound as claimed in claim 1 (wherein R^7 and R^8 together form a carbon-oxygen bond, R^9 and R^{10} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, R^{11} represents hydrogen and Y, R^5 and R^6 together represent an oxygen atom) or a tautomer thereof with a halogenating agent whereby a compound as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond and Y, R^5, R^6 and R^7 together represent a halogen atom) or a tautomer thereof is obtained.

37. A process for the preparation of compounds as claimed in claim 1 (wherein R^{11} represents hydrogen, R^9 and R^{10} together form a carbon-carbon bond, Y, R^5 and R^6 together represent an oxygen atom R^7 and R^8 together form a carbon-oxygen bond and R^4 represents hydrogen or phenyl) or a tautomer thereof which process comprises hydrolysing a compound as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents an oxygen atom without its lone pairs of electrons, R^7 and R^6 each represents a lone pair of electrons and R^5 represents C_{1-4} alkyl) or a tautomer thereof whereby a compound as claimed in claim 1 (wherein R^{11} represents hydrogen, R^9 and R^{10} together form a carbon-carbon bond, Y, R^5 and R^6 together represent an oxygen atom R^7 and R^8 together form a carbon-oxygen

bond and R^4 represents hydrogen or phenyl) or a tautomer thereof is obtained.

38. A process for the preparation of compounds as claimed in claim 1 [wherein R^8 and R_9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents a lone pair of electrons, R^5 represents C_{1-4} alkyl, optionally substituted phenyl, optionally substituted heteroaryl, hydroxy, aminothiocarbonyl, aminothiocarbonylamino or phenylamino, and R^6 represents hydrogen or C_{1-4} alkyl or R^5 and R^6 together represent the group $-(CH_2)_p-$ (wherein p is 4 or 5)] or a tautomer thereof which process comprises reacting a compound as claimed in claim 1 (wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents an oxygen atom without its lone pairs of electrons, R^7 and R^6 each represents a lone pair of electrons and R^5 represents C_{1-4} alkyl) or a tautomer thereof with an amine of the formula:



(VIII)

(wherein R^5 and R^6 are as herein defined) whereby a compound as claimed in claim 1 [wherein R^8 and R^9 together form a carbon-carbon bond, R^{10} and R^{11} together form a carbon-carbon bond, R^4 represents hydrogen or phenyl, Y represents a nitrogen atom without its lone pair of electrons, R^7 represents a lone pair of electrons, R^5 represents C_{1-4} alkyl, optionally substituted phenyl, optionally substituted heteroaryl, hydroxy, aminothiocarbonyl, aminothiocarbonylamino or phenylamino, and R^6 represent hydrogen or C_{1-4} alkyl or R^5 and R^6 together represent the group $-(CH_2)_p-$ (wherein p is 4 or 5)] or a tautomer thereof is obtained.

39. A process as claimed in any one of claims 18 to 38 wherein a compound of formula I obtained is converted into a salt thereof.

40. A process as claimed in any one of claims 18 to 38 wherein a salt of a compound of formula I obtained is converted into a compound of formula I.

41. A process as claimed in any one of claims 18 to 40 wherein the compound as claimed in claim 1 obtained is separated into its optically active isomers.

42. A process as claimed in any one of claims 18 to 41 substantially as herein described.

43. A process for the preparation of compounds as claimed in claim 1 substantially as herein described in any one of the Examples.

44. Compounds as claimed in claim 1 when prepared by a process as claimed in any one of claims 18 to 43.

45. Pharmaceutical compositions comprising as active ingredient at least one compound of formula I as defined in claim 1 or a physiologically compatible salt thereof in association with a pharmaceutical carrier or excipient.

46. Each and every novel composition, compound and process herein disclosed.

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